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Original Research Article

# Ophthalmic Manifestations of Hematopoietic Malignancy

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**Abstract**

**Background:** Hematological diseases encompass problems of plasma proteins, coagulation, and erythrocytes, leukocytes, and platelets. These conditions can either directly impact the eye or cause ophthalmic symptoms that develop later on in the illness. Ocular symptoms can frequently be the first sign of hematological disorders. The majority of individuals who present with ocular symptoms are symptomatic and need to see an ophthalmologist. Any area of the eye can be affected by hematological illnesses, and each disease may have a different set of symptoms. Intraretinal bleeding, cotton wool patches, and conjunctival pallor and hemorrhages are typical symptoms. It is not typical to have bleeding symptoms in the orbit, anterior segment, optic nerve, or retinal infiltrates.

**Aim:** To study the incidence of ocular involvement in systemic hematological disorders.

**Material and Method:** This prospective, non-interventional descriptive study was carried out in the ophthalmology department. The ophthalmology department evaluated forty patients with hematological problems. A proforma was created that had the following information: a brief medical history, an ocular history, anterior and posterior segment exams, and a hematological profile of the patient. Every patient received a thorough examination of the anterior and posterior segments, which included measurements of intraocular pressure, best corrected visual acuity, slit lamp assessment of the anterior segment, dilated retinal examination with an indirect, direct ophthalmoscope, and slit lamp biomicroscopy with a Volk 78 D lens. In cases when fundus photography was performed, good results were obtained. All participants gave their written, informed consent for the treatments and the use of the health information in their medical records.

**Results:** Ocular characteristics were discovered in 20 patients and 40 patients with hematological malignancies. Twelve women and 28 men made up the forty patients that were part in this study. Ocular findings were present in 14 of the 28 males and in 7 of the 12 females. A anterior segment finding was present in one male and one female among the ocular characteristics. There were 2 males and 2 females with neurological involvement. Analysis of the posterior segment revealed that it was involved more frequently than the anterior segment or neurological involvement, with findings found in 11 males and 4 females. With the exception of AML (acute myeloid leukemia), which had an equal frequency, and CML, where there was one case with anterior segment findings and one with posterior segment findings, the incidence of posterior segment findings was higher in each of the individual diseases than the incidence of anterior segment findings.

**Conclusion:** The ocular pathological findings in individuals being monitored for hematological malignancies are reported and evaluated in this study. Numerous cases demonstrate the potential for ocular involvement in these hematological illnesses as well as significant clinical symptoms that may be noted in each. Furthermore, these cases highlight the need of eye care for patients with hematologic malignancies, especially dry eye illness, given the development of innovative antineoplastic medicines that may increase life expectancy.

**Keywords:** Anemic retinopathy, Hematological disorders and Ocular manifestations.



## Introduction

Ocular symptoms are just one type of the many ailments that fall under the umbrella of hematological diseases. In fact, eye symptoms could be the first sign of a hidden hematological condition. One of the main health issues with a wide range of clinical presentations is blood diseases. Hematological abnormalities such as nutritional anemia are still frequent, particularly in third-world countries. In anemia, the retinal metabolism cannot withstand this prolonged lack of vital supplies without consequences, ultimately

succumbing to hypoxic damage. Therefore, anemia may be a sign of retinal injury that appears as pallor or bleeding. [1,2]

Ophthalmologists now have more opportunities to see patients with hematological malignancy that has spread to the central nervous system (CNS). [3,4] A recent analysis of multiple myeloma patients revealed that throughout the previous 20 years, the median survival duration had risen from 3 to 6 years. [5] There have only been 44 occurrences of orbital infiltrations in hematological cancer patients documented in the literature, making them extremely uncommon. [3, 6–7] The results of previous cases demonstrated that multiple myeloma's CNS involvement was not common. [8]

Up to 90% of individuals with hematological disorders may experience ocular symptoms. There is currently little information available in the literature about hematological disorders and ocular involvement. This might be because they seldom cause serious consequences and are uncommon in comparison to other ocular illnesses. These abnormalities may develop throughout the course of the disease or its treatment, or they may be the first sign of an underlying hematological problem. [9]

Leukemia is a malignant proliferative condition of hematopoietic bone marrow stem cells that is characterized by an abundance of immature neoplastic leukocytes in the bone marrow and a broad infiltration of these leukocytes into tissues, organs, and peripheral circulation. [10] It has long been known that leukemia can involve the eyes, and almost all ocular tissues can be impacted. Leukemia-related ocular involvement has been shown to occur in between 9% and 90% of cases. [11,12] Ocular involvement in leukemia may develop during the course of the illness or before the disease is diagnosed. [13]

It was previously thought that retinal damage had little bearing on prognosis in cases of acute leukemia. [14] Reports, however, now show that in cases of acute juvenile leukemia, ocular involvement is linked to a poor outcome. [15] According to Russo et al., the existence of particular orbital and ocular lesions was linked to a higher prevalence of bone marrow relapses and CNS involvement in both acute myelogenous leukemia (AML) and acute lymphocytic leukemia (ALL), which resulted in a worse survival rate. [16] When leukemia patients develop leukemic infiltrates, a systemic and neurological reevaluation must be done right away. [17]

Understanding the intraocular symptoms of leukemia and lymphomas is crucial due to the fact that these changes occur often and the eye frequently mirrors the body's disease condition. It's possible that the systemic sickness first manifests as eye symptoms. Indeed, the ophthalmologist was frequently called upon to assist in the diagnosis of leukemia prior to the advent of bone marrow biopsy. This may also apply to Indian patients, given the dearth of healthcare facilities outside of cities that are capable of treating hematological cancers. It is possible that the pattern of ocular illness in Indian individuals with hematological malignancies differs from research conducted in more developed nations. On the visual features in leukemic individuals, there is no research currently accessible from the Indian subcontinent. The purpose of this study was to assess the ocular abnormalities associated with hematological malignancies, anemia, and platelet problems.

## Material and Methods

This prospective, non-interventional descriptive study was carried out in the ophthalmology department. The ophthalmology department evaluated forty patients with hematological problems. A proforma was created that had the following information: a brief medical history, an ocular history, anterior and posterior segment exams, and a hematological profile of the patient. Every patient received a thorough examination of the anterior and posterior segments, which included measurements of intraocular pressure, best corrected visual acuity, slit lamp assessment of the anterior segment, dilated retinal examination with an indirect, direct ophthalmoscope, and slit lamp biomicroscopy with a Volk 78 D lens. In cases when fundus photography was performed, good results were obtained. All participants gave their written, informed consent for the treatments and the use of the health information in their medical records.

**Inclusion Criteria**:

- The patients who were referred to an ophthalmology op with hematological malignancies for ophthalmic evaluation.
- Those patients with haematologic malignancies registered in the oncology department.

**Exclusion Criteria:**

- Patients having diabetes, hypertension, dense cataractous changes, and other media opacities which prevented posterior segment examination.

**Study Criteria:** Every patient underwent a comprehensive ophthalmologic examination, which included schiotz tonometry, visual acuity testing, external ocular testing, and slit lamp testing. The history, physical examination, and neuroimaging using a computerized tomography (CT) scan were used to diagnose ocular-orbital cancers. A predetermined structure was followed for the gathering of data, which included the patient's

medical history, hematological data, and demographic profile. A comprehensive eye examination was carried out, comprising slit lamp biomicroscopy for the assessment of the anterior and posterior segments and a visual acuity assessment (VA) using the Snellen chart. VA < 20/40 was considered visual loss (VL). Indirect ophthalmoscopy was used to assess the posterior section following pupillary dilation with 1% Tropicamide eye drops. Unless the patient refused to cooperate for clinical photos, images of the anterior and posterior portions were only obtained for documentation. To measure intraocular pressure (IOP), an applanation tonometer was employed. Ocular hypertension was considered to be compatible with an IOP of 21 mmHg or above. The Dry Eye Work Shop criteria, the ocular surface disease index, tear production as measured by the 5-min Schirmer test, break-up time, and ocular surface staining were used to diagnose and stage dry eye disease (DED). After corneal coloration by fluorescence, the Schirmer test was conducted using sterile, anesthetic-treated strips, and the break-up time was recorded. After pupillary dilatation, the first examination of impaired patients was performed at the bedside, assessing the anterior chamber with a portable slit-lamp biomicroscope and the posterior chamber with direct ophthalmoscopy. All patients underwent blood smear examinations to determine the type of hematological malignancy they had. For a few chosen patients, a bone marrow examination was also performed.

**Statistical Analysis:** The association between ocular manifestations and hematological parameters was checked by Chi-square analysis and Fisher test. The overall significance level was set at 95% with $p < 0.05$ taken as statistically significant.

**Result:**

Twenty of the forty patients who had hematological malignancies had ocular characteristics. Twelve female patients and 28 male patients made up the forty patients that were part of this study. Seven of the twelve females and fourteen of the twenty-eight men had ocular characteristics.

**Table 1: Gender-related distribution of study subjects.**

| | Males | Females |
|---|---|---|
| Total cases | 28 | 12 |
| Ocular features | 14 | 7 |
| Anterior segment features | 1 | 1 |
| Posterior segment features | 11 | 4 |
| Neurological findings | 2 | 2 |

One man and one female had anterior segment findings among the ocular characteristics. Two males and two ladies had neurological involvement. Eleven males and four females had posterior segment results, indicating a higher frequency of posterior segment involvement compared to anterior section or neurological involvement.

**Table 2: Incidence of Ocular Features Among Individual Diseases.**

| Type of Disease | Ocular features | Anterior Segment | Posterior Segment |
|---|---|---|---|
| NHL | 2 | 0 | 1 |
| HD | 2 | 1 | 1 |
| MM | 4 | 2 | 2 |
| CML | 2 | 1 | 1 |
| CLL | 1 | 0 | 1 |
| AML | 3 | 1 | 2 |
| ALL | 5 | 1 | 4 |

The highest incidence of ocular characteristics among all the different hematological malignancies was seen in Chronic Myeloid Leukemia (CML), which was followed by an identical frequency of Acute Lymphatic Leukemia (ALL) and AML, at roughly 55.6% each. Hodgkin's disease (HD), with 9.1%, was the least common in the list. The remaining percentages were as follows: non-Hodgkin illness (25.5%), multiple myeloma (40.4%), and chronic lymphoid leukemia (CLL), which was 20%. With the exception of acute myeloid leukemia (AML), which had an equal frequency, and chronic myeloid leukemia (CML), where there was one case with anterior segment findings and one with posterior segment findings, the incidence of posterior segment findings was higher in each of the specific illnesses.

**Table 3: Types of retinal hemorrhage among study subjects**

| Types of Hemorrhage | In Leukemia's n = 14 | In Anemia's n = 5 |
|---|---|---|
| Flame | 98% | 70.32% |
| Roth spots | 47% | 40.75% |
| Deep | 74% | 55.12% |
| Pre-retinal | 10.40% | 23.50% |
| Subhyaloid | 10.40% | 13.21% |

Pre-retinal hemorrhage was present in 23.50% and sub-hyaloid hemorrhage in 10.40 % of cases. It was noted that among patients with Hb level < 4g%, all types of hemorrhages were present while deep and flame-shaped hemorrhages were more common in cases with a Hb range of 4-8 g% and > 8 g % respectively as shown in Table 3.

**Discussion**

Hematological diseases encompass problems of plasma proteins, coagulation, and erythrocytes, leukocytes, and platelets. These conditions can either directly impact the eye or cause ophthalmic symptoms that develop later on in the illness. Ocular symptoms can frequently be the first sign of hematological disorders. The majority of individuals who present with ocular symptoms are symptomatic and need to see an ophthalmologist. Any area of the eye can be affected by hematological illnesses, and each disease may have a different set of symptoms. Intraretinal bleeding, cotton wool patches, and conjunctival pallor and hemorrhages are typical symptoms. It is not typical to have bleeding symptoms in the orbit, anterior segment, optic nerve, or retinal infiltrates.

The prognosis for individuals with hematological malignancies has significantly improved due to advancements in diagnostic and therapeutic technologies. As a result, there is now more variation in ocular presentations, including how relapses are initially recognized as ocular presentations and therapeutic side effects. Numerous ocular tissues may be affected by any hematological malignancy, either directly through infiltration, by bleeding, through ischemia, or as a result of toxicity from different chemotherapy drugs. Ocular involvement can also occur in individuals receiving allogeneic bone marrow transplantation as a result of graft-versus-host reactions, or it can simply manifest as these patients' heightened vulnerability to infections due to immunosuppression. This can include endophthalmitis or just a basic case of bacterial conjunctivitis. Adnexa, conjunctiva, sclera, cornea, anterior chamber, iris, lens, vitreous, retina, choroid, and optic nerve disease can all be symptoms of these cancers. In order to determine the course and prognosis of the disease, it is also critical to recognize the variety of ocular appearances. [18]

Osama Badeeb et al.1995 [19] reported that Leukemia may affect any ocular tissue at some time during its course. The incidence of ocular involvement may be as high as 90%. Elise Torczynski et al.1983 [20] reported primary ophthalmic leukemia infiltrate in 3% and secondary ophthalmic findings in 39% and ocular changes unrelated to leukemia in 20% of their patients. Acute leukemias affect the eye four times as frequently as the chronic types.

In a study by Schachat et al.1989 [21], it was reported that Leukemic infiltrates were present in 3% of patients, other findings related to leukemia were seen in 39% of patients, and 20% of patients had unrelated abnormalities. Visual loss was seen in at least 5% of the patients. Shirley Fung et al2005 [22] in a study of 8 patients, six patients (75%) had known MM at the time of their ophthalmic evaluation, reported that ophthalmic manifestations of MM are uncommon and diverse. They may appear at the initial presentation of the disease or occur late in the disease process.

Paris A et al.2002 [23] in a study found that the most frequent ocular findings were seen in the conjunctiva (33.4%). 15.4% of patients presented with posterior segment findings, without loss of ocular acuity. Other manifestations were dry eye syndrome and proptosis.

Early DED detection and therapy are crucial for reducing eye damage in a multidisciplinary manner. Reduced ocular surface irritation, lubrication and tear preservation, and prevention and control of tear evaporation are the three therapy techniques. The initial course of treatment is still topical lubrication, with viscous ointments added as a supplement to tear replacements. Treatment options include eyewear and contact lenses, dietary and environmental modifications, and a variety of pharmaceutical medications.

When ophthalmologic involvement is detected early, visual function can be restored. Steroid and systemic therapy improved the ocular state in four of our instances. Patients with favorable ophthalmologic prognostic characteristics exhibited higher life periods than instances with poor ophthalmologic prognosis. Consequently, early detection of ophthalmologic involvement is likely critical for enhancing patients' prognosis when dealing with hematological malignancy.

## Conclusion

The ocular pathological findings in individuals being monitored for hematological malignancies are reported and evaluated in this study. Numerous cases demonstrate the potential for ocular involvement in these hematological illnesses as well as significant clinical symptoms that may be noted in each. The existence of posterior segment lesions in leukemia patients served as a notable example of this. Furthermore, these cases highlight the need of eye care for patients with hematologic malignancies, especially dry eye illness, given the development of innovative antineoplastic medicines that may increase life expectancy. Our results thus validate the need for routine ocular evaluation both prior to and throughout treatment.

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