DOI: 10.7860/JCDR/2024/69407.19293

Original Article

Ophthalmology Section

Ocular Manifestations of Leukaemia: A Cross-sectional Study from Tertiary Care Hospital of South Gujarat, India

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ABSTRACT

Introduction: Leukaemic ophthalmopathy can be either symptomatic or asymptomatic. Several factors can cause leukaemic ophthalmopathy, including opportunistic infections, direct ocular infiltration by leukaemic cells, indirect ocular involvement from subsequent haematologic alterations, and consequences from different treatment modalities. Patients with leukaemia who develop leukaemic infiltrates must undergo urgent systemic and neurological re-evaluation.

Aim: To evaluate the prevalence and spectrum of leukaemic ophthalmopathy among leukaemic patients and to identify and analyse the common ocular manifestations of leukaemia in different age and gender groups.

Materials and Methods: A cross-sectional study was conducted at a tertiary care hospital in South Gujarat, India. A total of 48 patients diagnosed with leukaemia were included in the study. Detailed histories regarding their systemic illness, present systemic complaints, ocular complaints, and history of treatment were noted. Detailed ophthalmoscopic examinations like slit lamp examinations, fundoscopic examinations, visual acuity, and intraocular pressure were performed on each participant. Statistical analysis was conducted using descriptive data analysis methods in Microsoft Excel sheets.

Results: Out of the total 48 leukaemia patients recruited, 16 (33.33%) had ocular manifestations. Among the 25 acute leukaemia patients and 23 chronic leukaemia patients, 8 (32%) and 8 (34.78%) had ocular manifestations, respectively. Among all ocular manifestations, venous tortuosity was the most common, followed by deep and superficial retinal haemorrhage, dry eye, and Roth's spot.

Conclusion: The prevalence of ocular manifestations in leukaemia was reported to be 33.33%. Although an ophthalmologist's involvement in leukaemia treatment is secondary, it is nonetheless crucial to promptly recognise any ocular signs due to the worse prognosis associated with ocular involvement and to rule out extramedullary disease.

Keywords: Eye and leukaemia, Leukaemia complications, Leukaemic retinopathy, Orbital infiltrate

INTRODUCTION

The malignant proliferative illness known as leukaemia, affects haematopoietic bone marrow stem cells. It is characterised by the overabundance of immature neoplastic leukocytes in the bone marrow and their extensive infiltration of organs, tissues, and peripheral blood [1]. Furthermore, the increasing survival rates of leukaemia patients have led to a rise in the diversity of ocular manifestations as a consequence. The reported occurrence of ocular involvement in leukaemia ranges from 9% to as high as 90% [2,3]. Ocular involvement in leukaemia may develop during the course of the illness or before the disease is diagnosed. After the meninges and testicles, orbital and ocular lesions have been reported as the third most common extramedullary site of acute leukaemias [4]. Therefore, it is important to closely examine the sites of extramedullary leukaemic infiltration. The natural history and survival prognosis of systemic leukaemia are significantly influenced by ophthalmic involvement, which is associated with significant ocular morbidity and vision loss. Recent findings have shown a negative correlation between the prognosis for acute childhood leukaemia and the presence of ocular involvement [5]. Hence, it is critical to consider an ocular evaluation when diagnosing acute leukaemia in both adults and children.

Leukaemic ophthalmopathy can be either symptomatic or asymptomatic. It can be caused by leukaemic cells directly invading the eye, indirect ocular involvement from subsequent haematologic alterations, opportunistic infections, and issues from different treatment techniques. The presence of specific orbital and ocular lesions have been associated with a higher frequency of bone marrow relapses and Central Nervous System (CNS) involvement, leading to a lower survival rate [6]. When leukaemia patients develop leukaemic infiltrates, an urgent systemic and neurological re-evaluation must be conducted. Therefore, it is crucial to consider performing an ocular examination on every leukaemic patient.

Few studies have been conducted to assess the rate of ocular manifestations in leukaemia [4,6-10]. Due to insufficient data on this topic from our country, this study was conducted to determine the pattern of ocular findings related to leukaemia. Additionally, this subject has not been investigated in this locality. Thus, the aim of the study was to evaluate the prevalence and spectrum of leukaemic ophthalmopathy among all new and follow-up leukaemia patients coming to a tertiary care hospital in South Gujarat, India.

MATERIALS AND METHODS

This cross-sectional study was conducted at a tertiary care centre in South Gujarat, India (Government Medical College and New Civil Hospital, Surat) and its attached cancer institute from December 2015 to December 2016. The study was approved by the Institutional Human Research Ethics Committee with the assigned number MCS/STU/ETHICS/Approval/26040/15.

Inclusion criteria: All diagnosed leukaemia patients admitted to the tertiary care hospital in South Gujarat who were willing to participate in the study were included and prospectively analysed.

Exclusion criteria: Patients with a history of ocular diseases that hinder adequate fundus visualisation (such as dense cataracts, corneal opacity), patients under the age of 1.5 years, and patients with ocular manifestations due to other systemic diseases (such as diabetes mellitus, hypertension, sickle cell disease, etc.,) were excluded from the study.

Sample size calculation: Based on observations from the previous year, where approximately 40-50 leukaemia patients attended the tertiary care hospital and attached cancer institute, this study aimed to investigate ocular findings in leukaemia patients. The sample size was arbitrarily set at 48 based on clinical observations. A total of 48 patients who met the inclusion and exclusion criteria were included in the study. Informed written consent was obtained from the participants or their legal guardians before inclusion in the study.

At the time of inclusion in the study, detailed participant history, including demographic data, systemic illness history, current systemic and ocular complaints, and treatment history, were recorded. Patients' visual acuity was assessed using a Snellen chart. An ocular examination was conducted using a Carl Zeiss Meditech AG slit lamp. Fundus examination was performed using a Heinz direct ophthalmoscope and an indirect ophthalmoscope with a +20 D aspheric lens under full mydriasis. Tropicamide (0.8%) and phenylephrine (5%) eye drops were used to achieve mydriasis. Intraocular pressure was measured using a Goldmann Applanation tonometer and a non contact tonometer in children. Details of blood investigations, such as complete blood count and differential blood cell count, were recorded. B scans and reviewed computed tomography scans of the brain and orbit reports of patients were also utilised when necessary.

STATISTICAL ANALYSIS

Statistical analysis was conducted using descriptive data analysis methods in Microsoft Excel sheets.

RESULTS

A total of 48 participants who met the inclusion and exclusion criteria over 12 months were examined for ocular changes during the study period. The age of these patients ranged from 1.5 years to 70 years, with a mean age of 30.14±19.36 years. Out of the 48 patients, 16 (33.33%) were in the children group, aged between 1.5 years to 15 years. Additionally, 9/48 (18.75%) were in the 16-30 years age group, 11/48 (22.92%) in the 31-45 years age group, and 12/48 (25%) in the >45 years age group. The gender distribution showed that 30/48 (62.5%) patients were male and 18/48 (37.5%) were female, with a male-to-female ratio of 1.67:1. In this study, the highest incidence was of Acute Lymphocytic Leukaemia (ALL), with 24/48 (50%) cases. The incidence of Chronic Myeloid Leukaemia (CML), Chronic Lymphocytic Leukaemia (CLL), and Acute Myeloid Leukaemia (AML) were 19/48 (39.58%), 4/48 (8.33%), and 1/48 (2.08%), respectively. Among the participants, 16/48 (33.33%) had ocular manifestations. Gender-wise distribution showed that 11 (36.67%) males and 5 (27.78%) females had ocular manifestations. The frequency of ocular manifestations and their relationship with various parameters such as age, gender, type of leukaemia, platelet count, and White Blood Cell (WBC) count are presented in [Table/Fig-1].

Parameters	Number of patients (total-48), n (%)	Numbers of patients with ocular manifestations (total-16), n (%)
Age of patients (years)		
1.5 to 15	16 (33.33)	5 (31.25)
16 to 30	9 (18.75)	4 (44.44)
31 to 45	11 (22.92)	3 (27.27)
>45	12 (25)	4 (33.33)
Gender		
Male	30 (62.50)	11 (36.66)
Female	18 (37.50)	5 (27.77)
Different classes of leukaemia		
Acute	25 (52.08)	8 (32)
Chronic	23 (47.92)	8 (34.78)
Different types of leukaemia		
ALL	24 (50)	7 (29.17)
AML	1 (2.08)	1 (100)
CLL	4 (8.33)	4 (100)
CML	19 (39.58)	4 (21.05)
Platelets (cells/cumm)		
<50,000	7 (14.58)	7 (100)
50,000-1,50,000	19 (39.58)	5 (26.31)
>1,50,000	22 (45.83)	4 (18.18)
White Blood Cells (cells/cumm)		
<4000	19 (39.58)	9 (47.36)
4000-11000	23 (47.91)	3 (13.04)
11000-25000	1 (2.08)	0
>25000	5 (10.41)	4 (80)

[Table/Fig-1]: Frequency of ocular manifestations and their relationship with various parameters.
ALL: Acute lymphocytic leukaemia; AML: Acute myeloid leukaemia; CLL: Chronic lymphocytic leukaemia; CML: Chronic myeloid leukaemia

In this study, the patients were divided into three groups based on the duration since their diagnosis of leukaemia. The incidence of ocular manifestations was highest in patients diagnosed more than two years ago, with 7 (43.75%) cases [Table/Fig-2].

Types of leukaemia	Duration					
	<6 months		6 months to 2 years		>2 years	
	Total patients	Ocular findings	Total patients	Ocular findings	Total patients	Ocular findings
ALL	6	3	13	3	5	1
AML	1	1	0	0	0	0
CLL	0	0	0	0	4	4
CML	6	1	6	1	7	2
Total	13	5	19	4	16	7

[Table/Fig-2]: Incidence of ocular manifestations according to duration of leukaemia.
ALL: Acute lymphocytic leukaemia; AML: Acute myeloid leukaemia; CLL: Chronic lymphocytic leukaemia; CML: Chronic myeloid leukaemia

This study shows that out of the 16 patients with ocular manifestations, 6 (37.5%) patients had 6/6 visual acuity on the Snellen's chart. Additionally, 2 (12.5%) patients had visual acuity ranging from 6/18 to 6/9, and 2 (12.5%) patients had visual acuity between 6/60 to 6/24, which was attributed to refractive errors rather than ocular findings related to leukaemia. Among these 10 patients with vision better than 6/60, ocular findings included dry eye with meibomitis, conjunctivitis, tortuous retinal vessels, and subconjunctival haemorrhages, none of which resulted in a decrease in vision. In addition, among the 4 (25%) patients with vision ranging from 1 MFC to 6 MFC, two patients had subhyaloid haemorrhage, one patient had papilledema in both eyes, and one had retinal infiltrates. Out of the 2 (12.5%) patients with visual acuity less than 1 MFC, one patient had vitreous haemorrhage in both eyes, and the other had central retinal artery occlusion with proptosis due to orbital infiltration in one eye and papilledema in the other eye [Table/Fig-3].

The various ocular manifestations of leukaemia observed in this study are detailed in [Table/Fig-4]. These changes are categorised into primary and secondary changes. It was noted

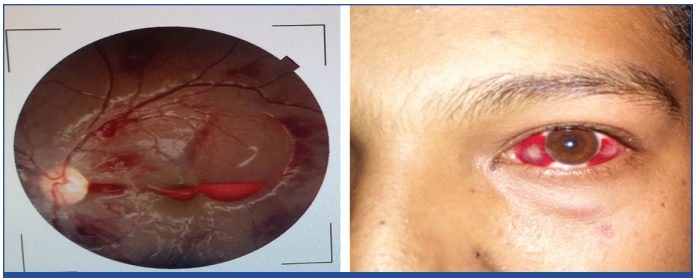
Visual acuity	n (%)
6/6	6 (37.5)
6/18 to 6/9	2 (12.5)
6/60 to 6/24	2 (12.5)
1 MFC* TO 6 MFC	4 (25)
<1 MFC	2 (12.5)

[Table/Fig-3]: Visual acuity in patients having ocular manifestations.
*MFC: Meter finger counting

Ocular findings in leukaemia	n (%)
Primary changes	
Proptosis due to orbital infiltration	1 (2.08)
Choroidal infiltration (exudative retinal detachment)	1 (2.08)
Secondary changes	
Orbital cellulitis	1 (2.08)
Conjunctivitis	1 (2.08)
Subconjunctival haemorrhage	1 (2.08)
Dry eye	4 (8.33)
Papilloedema	2 (4.2)
Superficial retinal haemorrhage	6 (12.5)
Deep intraretinal haemorrhage	7 (14.58)
Roth's spot	3 (6.25)
Dilated/tortuous veins	11 (22.92)
Subhyaloid haemorrhage	2 (4.2)
Vitreous haemorrhage	1 (2.08)

[Table/Fig-4]: Incidence of various ocular manifestations in leukaemia.

that some patients exhibited multiple ocular findings, such as retinal haemorrhages, subhyaloid haemorrhage [Table/Fig-5], subconjunctival haemorrhage [Table/Fig-6], or papilledema, along with dilated/tortuous vessels.



[Table/Fig-5]: Fundus photograph of a seven-year-old male patient with Acute Lymphocytic Leukaemia (ALL) showing subhyaloid haemorrhage with superficial retinal haemorrhages. **[Table/Fig-6]:** A 20-year-old male patient with Acute Lymphocytic Leukaemia (ALL) showing subconjunctival haemorrhages. (Images from left to right).

DISCUSSION

In this study, a total of 48 patients with leukaemia were examined. The prevalence of ocular manifestations in leukaemia was reported to be 33.33%. The mean age was 30.14±19.36 years, which was comparable to Guyer DR et al., (mean age 33.3 years), Reddy SC and Jackson N (mean age 34.6 years), and Mirshahi R et al., (mean age 27.6±17.9 years) in their studies on leukaemia [7-9]. This study cohort exhibited a predominance of males, with 30 males (62.5%) out of 48 patients. This finding was similar to the study by Koshy J et al., where there were 61 (63.54%) males out of a total of 96 patients, and 35 (36.46%) females [10]. The observed distribution of sex could be attributed to the natural sex prevalence pattern of leukaemia or the established gender inequality favouring males in healthcare access, or a combination of both factors. This suggests the importance of identifying and addressing gender-related barriers to healthcare access, with significant implications for healthcare planners and implementers [10].

The prevalence of ocular manifestations in leukaemia has been reported between 9-90% in various studies [2,3]. This divergent variation in results may be due to the transient nature of ocular findings, which may wax and wane with time and treatment. The present study was a cross-sectional hospital-based study that includes all types of leukaemia patients visiting the outpatient departments of the ophthalmology department and cancer institute. In this study, 16 (33.33%) out of 48 patients had ocular findings, which was comparable to findings from other studies. Reddy SC and Jackson N conducted a study on 288 patients, of which 102 (35.4%) patients with leukaemia exhibited ocular manifestations [8]. Mirshahi R et al., studied 85 patients, with 27 (31.8%) showing ocular findings [9]. Koshy J et al., examined a total of 96 patients, among whom 42 (43.8%) patients had ocular findings [10]. Although the sample size of these studies was larger than the present study, the results of both studies were similar.

Different types of leukaemia exhibit varying tendencies to develop ophthalmic symptoms, as observed in this study. In a study by Reddy SC and Jackson N out of 288 cases, 102 (35.5%) acute leukaemia patients presented with ocular manifestations [8]. In Koshy J et al., study, 35/68 (51.9%) acute and 7/28 (25%) chronic leukaemia patients had ocular findings [10]. This disparity could stem from different study designs or may genuinely reflect the nature of the illness. The transient nature of the disease or its complications may contribute to this variability across studies.

Upon comparing different types of acute and chronic leukaemia, this study observed that 29.17% of ALL patients had ocular findings, which aligned closely with previous findings. Reddy SC and Jackson N reported 30.3% of ocular manifestations in ALL patients [8], and Koshy J et al., noted ocular manifestations in 32% of ALL patients [10]. In the present study, all patients (N=1, 100%) with AML exhibited ocular manifestations. However, due to its very small size, no statistically significant observations could be drawn. Additionally, all 4 (100%) patients with CLL presented with ocular manifestations. In CML, 21.05% of patients had ocular manifestations. Koshy J et al., study reported 27.8%, and Reddy SC and Jackson N study documented 39.5% of patients with CML developing ocular manifestations [10]. This discrepancy could arise from differing study designs or may indeed reflect the nature of the disease. The comparison of this study is illustrated in [Table/Fig-7] [8-11].

S. no.	Author's name and publication year	Place of study	Number of subjects	Objective	Conclusions (ocular involvement %)
1	Present study, 2024	South Gujarat, India	48	Evaluate the ocular manifestations in leukaemia	16 (33.33)
2	Reddy SC and Jackson N, 2004 [8]	Malaysia	288	Ocular involvement in leukaemia	102 (35.4)
3	Mirshahi R et al., 2022 [9]	Iran	85	To present primary ocular manifestations in acute leukaemia	27 (31.8)
4	Koshy J et al., 2015 [10]	Punjab, India	96	Ophthalmic manifestations of acute and chronic leukaemias presenting to a tertiary care centre in India	42 (43.8)
5	Ilo OT et al., [11] 2019	Nigeria	160	Ocular manifestations of leukaemia a teaching hospital experience	56 (35)

[Table/Fig-7]: Comparison of various studies [8-11].

The platelet count and ocular findings in various patients indicated that those with lower platelet counts exhibited more ocular findings. This can be attributed to an increased generalised tendency to bleed associated with thrombocytopenia. Thrombocytopenia may result from the adverse effects of chemotherapy, leading to bone marrow suppression [12]. In this study, patients with both leukocytopenia and leukocytosis presented ocular manifestations. A high White Blood Cell (WBC) count can also induce hyper viscosity, potentially causing venous tortuosity [13]. Individuals with leukaemia are susceptible to developing uncommon and potentially life-threatening infections during periods of neutropenia, resulting from both the underlying disease and chemotherapy. These patients are at risk of a wide range of infections by viral,

fungal, protozoal, and bacterial agents, which can lead to orbital cellulitis in the eye [14,15]. This indicates that both leukopenia and leukocytosis may contribute to the occurrence of ocular manifestations in leukaemia.

Out of a total of 16 patients, two patients exhibited primary or direct leukaemic infiltration, presenting as proptosis due to orbital infiltration and exudative retinal detachment caused by choroidal infiltration. Several studies have reported exudative retinal detachment as the initial ocular sign of leukaemia [16,17]. The remaining 14 patients showed secondary involvement, such as orbital cellulitis, conjunctivitis, dry eye, subconjunctival haemorrhage, venous tortuosity, and vitreous haemorrhage. The principal manifestations of leukaemic involvement can be explained by factors like thrombocytopenia, blood viscosity, leukocytosis, secondary infections, or various leukaemia treatments. Chemotherapy and radiotherapy, for example, may lead to dry eye, bone marrow suppression, and pancytopenia [15,18,19]. Prior to the advent of modern chemotherapy, significant infiltrations were frequently observed, partially or completely destroying retinal architecture [2]. Ocular and orbital lesions have been reported as the third most frequent extramedullary locations of acute leukaemias after the meninges and testicles [4]. Therefore, it is crucial to closely examine the sites of extramedullary leukaemic infiltration, not only due to their local morbidity but also because these sites may serve as a reservoir for the proliferation of leukaemic cells, potentially leading to systemic relapse.

Limitation(s)

There were a few limitations to this study. Firstly, there were not enough patients with AML in this study to draw firm conclusions. Secondly, not all individuals underwent routine ocular ultrasonography, computed tomography, or magnetic resonance imaging to check for choroidal involvement of leukaemia.

CONCLUSION(S)

The prevalence of ocular manifestations in leukaemia was reported to be 33.33%. The most frequent ocular abnormalities associated with leukaemia were secondary or indirect involvement of the posterior segment. Although an ophthalmologist's involvement in leukaemia treatment is secondary, it is nonetheless important to promptly recognise any ocular signs due to the worse prognosis linked to ocular involvement and to rule out extramedullary disease.

Upon diagnosis and then at least every six months afterward, all patients with leukaemia should undergo an ocular examination. Even though ocular involvement may serve as an early indicator of CNS disease or a recurrence, many individuals do not exhibit any symptoms. Authors propose that complete cooperation between physicians, oncologists, and ophthalmologists is necessary, and patients suspected of having eye symptoms should be promptly evaluated by an ophthalmologist.

REFERENCES

[1] Catovsky D. Chronic lymphocytic leukaemias and other leukaemias of mature B and T cells. In: Weatheral DJ, Ledingham JG, Warrel DA, editors. Oxford Textbook of Medicine. Oxford: Oxford University Press; 1996. Pp. 3419-22.
[2] Kincaid MC, Green WR. Ocular and orbital involvement in leukaemia. Surv Ophthalmol. 1983;27(4):211-32.
[3] Leonardy NJ, Rupani M, Dent G, Klintworth GK. Analysis of 135 autopsy eyes for ocular involvement in leukaemia. Am J Ophthalmol. 1990;109(4):436-44.
[4] Charif Chefchaouni M, Belmekki M, Hajji Z, Tahiri H, Amrani R, El Bakkali M, et al. Ophthalmic manifestations of acute leukaemia. J Fr Ophtalmol. 2002;25(1):62-66.
[5] Ohkoshi K, Tsiaras WG. Prognostic importance of ophthalmic manifestations in childhood leukaemia. Br J Ophthalmol. 1992;76(11):651-55.
[6] Russo V, Scott IU, Querques G, Stella A, Barone A, Delle Noci N. Orbital and ocular manifestations of acute childhood leukaemia: Clinical and statistical analysis of 180 patients. Eur J Ophthalmol. 2008;18(4):619-23. Doi: 10.1177/112067210801800420. PMID: 18609485.
[7] Guyer DR, Schachat AP, Vitale S, Markowitz JA, Braine H, Burke PJ, et al. Leukaemic retinopathy. Ophthalmology [Internet]. 1989;96(6):860-64.
[8] 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.1600-0420.2003.00197.x. PMID: 14738490.
[9] Mirshahi R, Ghassemi F, Koochakzadeh L, Faranoush M, Ghomi Z, Mehrvar A, et al. Ocular manifestations of newly diagnosed acute leukaemia patients. J Curr Ophthalmol. 2022;34(1):100-05.
[10] Koshy J, John MJ, Thomas S, Kaur G, Batra N, Xavier WJ. Ophthalmic manifestations of acute and chronic leukaemias presenting to a tertiary care center in India. Indian J Ophthalmol. 2015;63(8):659-64.
[11] Ilo OT, Adenekan AO, Alabi AS, Onakoya AO, Aribaba OT, Kehinde MO, et al. Ocular manifestations of leukaemia: A teaching hospital experience. Niger Postgrad Med J. 2019;26(4):205-10. Doi: 10.4103/npmj.npmj_50_19. PMID: 31621659.
[12] Chennamadhavuni A, Lyengar V, Mukkamalla SKR, Shimanovsky A. Leukaemia. [Updated 2023 Jan 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
[13] Gertz MA. Acute hyperviscosity: Syndromes and management. Blood. 2018;132(13):1379-85. Doi: 10.1182/blood-2018-06-846816. Epub 2018 Aug 13. PMID: 30104220; PMCID: PMC6161773.
[14] Bagheri A, Abrishami A, Karimi S. Acute myelogenous leukaemia mimicking fulminant periorbital cellulitis. J Ophthalmic Vis Res. 2013;8(4):380-82. PMID: 24653827; PMCID: PMC3957046.
[15] Lakhkar BN, Banavali S, Philip P. Orbital granulocytic sarcoma in acute myelogenous leukaemia. Indian J Pediatr. 2000;67(3):234-35.
[16] Hine JE, Kingham JD. Myelogenous leukaemia and bilateral exudative retinal detachment. Compr Ther. 1979;5(2):55-58. PMID: 284876.
[17] Primack JD, Smith ME, Tychsen L. Retinal detachment in a child as the first sign of leukemic relapse: Histopathology, MRI findings, treatment, and tumor-free follow up. J Pediatr Ophthalmol Strabismus. 1995;32(4):253-56.
[18] Tyagi M, Agarwal K, Paulose RM, Rani PK. Retinal haemorrhages: A clue to the underlying leukaemia. BMJ Case Rep. 2017;2017:bcr2017219741. Doi: 10.1136/bcr-2017-219741. PMID: 28951507; PMCID: PMC5747617.
[19] Nuzzi R, Trossarello M, Bartoncini S, Marolo P, Franco P, Mantovani C, et al. Ocular complications after radiation therapy: An observational study. Clin Ophthalmol. 2020;14:3153-66. Doi: 10.2147/OPTH.S263291. PMID: 33116366; PMCID: PMC7555281.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 03, 2024
- Manual Googling: Feb 08, 2024
- iThenticate Software: Mar 13, 2024 (12%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jan 03, 2024**
Date of Peer Review: **Jan 20, 2024**
Date of Acceptance: **Mar 15, 2024**
Date of Publishing: **Apr 01, 2024**