Ocular manifestations and factors associated with haematological malignancies at two tertiary hospitals in Tanzania

Gomba S[1,2], Nyamita O[3], Mhina C[2], Mosenene S[2] , Frank Sandi F[1], Mafwiri MM[2]

[1]School of Medicine and Dentistry, Department of Surgery, University of Dodoma, Tanzania
[2]Department of ophthalmology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
[3]Muhimbili National Hospital, Dar es Salaam, Tanzania

Corresponding author: Dr Sophia Gomba, Department of Ophthalmology, School of Medicine and Dentistry, The University of Dodoma, P.O. Box 259, Dodoma, Tanzania, Email: Sophiagomba6@gmail.com

ABSTRACT

Backgroud: Ocular involvement in haematological malignancy may profoundly affect the visual outcome of survivors, although little about this is known in our setting. Haematological malignancies include lymphoma, leukemia, and multiple myeloma. Ocular manifestations may be the initial diagnostic symptoms or the earliest identifiers for relapse or progression of haematological malignancies. Ocular involvement can result from direct malignant infiltration or indirect sequel of haematological cellular derangement.
Objective: This study aims to determine the burden of ophthalmic manifestations, describe the manifestations and the factors associated with haematological malignancies among patients attending Muhimbili National Hospital (MNH) and Ocean Road Cancer Institute (ORCI) in Dar es Salaam.
Methods: Hospital-based cross-sectional study at MNH and ORCI from June 2021 to January 2022. Patients who met the inclusion criteria were recruited consecutively. Data analysis was done with SPSS version 23.
Results: A total of 99 patients with haematological malignancies were recruited, 61.6% were males. The age range was 2 to 77 years with a mean age of 29 years. Two-thirds (61.6%) of the participants had ophthalmic manifestations. Posterior segment manifestations were the most common with roth spots (31.1%) and intraretinal haemorrhage (21.0%) as the most frequent presentations. Vision-threatening manifestations such as sub-hyaloid haemorrhage and optic nerve swelling were present in 6.7% and 11.1% of patients respectively. Direct infiltration was present in 15.15% of the patients. Low haemoglobin level was the statistically significant factor associated with ocular involvement among the study participants.
Conclusion: The prevalence of ophthalmic manifestations of haematological malignancies at MNH and ORCI was significantly high. Roth spots and intraretinal haemorrhages were the most common manifestations. Direct malignant ocular infiltrations were present in a few patients. Patients with haemoglobin level of 8g/dl or less had four times increased odds of having ocular manifestations. A comprehensive ophthalmic exam needs to be done for all patients with haematological malignancies for early detection and intervention.

Key words: Ocular manifestation, Leukemia, Lymphoma, Multiple myeloma

INTRODUCTION

Haematological malignancies are cancers that originate in the blood-forming tissues which are the bone marrow and lymphoid tissue. They account for 6.5% of all cancers globally, with 25% of the burden in sub-Saharan Africa[1]. Haematological malignancies account for 10% of the malignancies diagnosed in sub–Saharan Africa[2]. They are mainly classified into three types which are leukemia, lymphoma, and multiple myeloma[3]. Non-Hodgkin's lymphoma is the most common haematological malignancy in western Tanzania and sub-Saharan Africa[1,4].

Ocular manifestations of haematological malignancies are features that occur in any part of the eye as a result of haematological malignancy and may be caused by direct malignant infiltration, or as a result of haematological cellular derangements. They may be the initial presenting symptoms of haematological malignancies or the first site for detection of disease relapse. The prognostic significance of ocular manifestation of haematological malignancy is important as it may signify involvement of the central nervous system[5]. The global prevalence of ocular manifestations among patients with haematological malignancies ranges from 6 to 90%, with majority of affected individuals in developing countries[6,7].

Different types of haematological malignancies may present with similar haematological derangements. It is postulated that in cases of acute myeloid leukemia and acute lymphoid leukemia, anaemia, thrombocytopenia, and leukocytosis may be the factors predicting the occurrence of ocular manifestations[5,8]. There is a paucity of information on the relationship between haematological malignancies and ocular manifestations in sub-Saharan Africa.

This study aimed to assess the proportion, clinical manifestations, and factors associated with haematological malignancies at Muhimbili National Hospital, Haematology and Ophthalmology Units and Ocean Road Cancer Institute in urban Tanzania.

MATERIALS AND METHODS

Study design and setting: This was a hospital-based cross-sectional study, conducted for a period of 7 months from June 2021 to January 2022 at two tertiary hospitals, Muhimbili National Hospital Haemato-oncology and Ophthalmology Units and Ocean Road Cancer Institute, Haemato-oncology Unit in Dar es Salaam, Tanzania.

Inclusion criteria: A consecutive sampling technique was used to recruit participants with a confirmed diagnosis of haematological malignancy before initiation of treatment.

Exclusion criteria: Patients with comorbidities such as HIV, diabetes mellitus, hypertension, and other malignancies were excluded as these diseases may have overlapping ophthalmic manifestations with haematological malignancies. Patients with dense cataracts that may have precluded posterior segment examination were also excluded.

Sample size: The minimum estimated sample size was 98 and it was calculated using the sample size calculation formula for finite population. The study population size which was used for calculation was 154, obtained from the 2020 oncology registry and a proportion of ophthalmic manifestations of 77.7% from a study done in Nigeria in 2010 with a marginal error of 5%[9].

Data collection procedure: Data was collected using a researcher-administered questionnaire at the haemato-oncology clinics and wards. For children aged 6 years and above, written assent was obtained in addition to informed consent from their parents. For children of less than 6 years of age, very sick adults and adult patients, informed written consent was obtained from their parents or guardians, caretakers and the patients respectively. Interviews were carried out by the principal investigator to obtain the patients' demographic data. Information on the particular malignancy including haematological parameters, bone marrow aspiration cytology results, and biopsy results were obtained from the patients' files.

The ocular examination included a visual acuity assessment followed by ophthalmic examinations of the external and anterior segment which were performed using a torch and portable slit lamp biomicroscope. An indirect ophthalmoscopy examination was performed using an overhead indirect ophthalmoscope with a 20D lens after pupillary dilatation with 1% tropicamide eye drops. All data was collected and recorded using a pretested questionnaire.

Data analysis: Data was analyzed using the Statistical Package for Social Science (SPSS) version 23. Frequency distribution tables for demographic data, type of malignancy and type of ophthalmic manifestations were generated. The chi-squared test was used to assess the associations present, with a p-value of less than 0.05 used as a maximum marginal error of statistically significant associations. Logistic regression analysis assessed the independent associated factors of ophthalmic manifestations.

Ethical consideration: Ethical approval was obtained from the Muhimbili University of Health and Allied Sciences, (MUHAS) institution review board. The permission to conduct the study was obtained from the Research and Publication Department of Muhimbili National Hospital and Ocean Road Cancer Institute.

RESULTS

A total of 99 patients diagnosed with haematological malignancies were enrolled in the study. Majority of the patients were males (61.6%), with a male to female ratio of 1.6:1. The majority (64.7%) of patients were adults with a median age of 29 years, (Table 1).

Table 1: Demographic characteristics of the study participants (N= 99)

Characteristic	Frequency	
	No.	(%)
Sex		
Male	61	61.6
Female	38	38.4
Age (years)		
0-17	35	35.4
≥18	64	64.7
Median (Range)	29 (4, 77)	
Level of education		
Nonformal	6	6.1
Pre-school	9	9.1
Primary	33	33.3
Secondary	20	20.2
College	31	31.3
Occupation		
Employed	32	32.2
Self-employed	25	25.3
No job	42	42.4

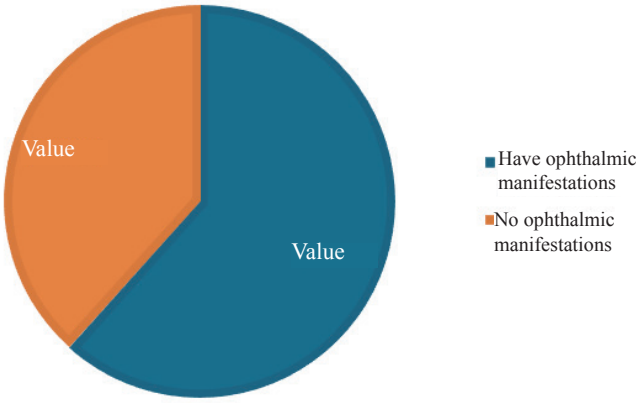
Table 2: Clinical characteristics of the study participants (N=99)

Characteristic	Frequency	
	No.	(%)
Type of haematological malignancy		
ALL	26	26.3
AML	34	34.3
CML	12	12.1
HL	2	2.0
NHL	11	11.1
MM/Plasmacytoma	14	14.1
Total WBC count($\times 10^9$/L)		
≤3	18	18.2
4-11	31	31.3
>11	50	50.5
Platelet level($\times 10^9$/L)		
<150	67	67.7
150-450	26	26.3
>450	6	6.1
RBC($\times 10^{12}$/L)		
<4	73	73.7
4-6	26	26.3
Haemoglobin level(g/dl)		
≤8	66	66.7
8.1-11	23	23.2
>11	10	10.1

AML=Acute Myeloid Leukemia, ALL=Acute Lymphoblastic Leukemia, CML=Chronic Myeloid Leukemia, HL=Hodgkin Lymphoma. NHL=Non-Hodgkin lymphoma. MM= Multiple Myeloma

Acute myeloid leukemia was the most common haematological malignancy (34.3%). Half (50.5%) of the patients had a leukocytosis (WBC count > than 11×10^9/L), two-thirds (67.7%) of patients had thrombocytopenia (platelet count <150 x10^9/L) and most of the patients (66.7%) had anaemia (haemoglobin level of less or equal to 8g/dl), (Table 2). The proportion of ocular manifestations among patients with haematological malignancy at Muhimbili National Hospital and Ocean Road Cancer institute was 61.62% of the participant (Figure 1).

Figure 1: Proportion of ophthalmic manifestations among patients with haematological malignancies at MNH and ORCI (N=99)



Majority (75.90%) of the patients had normal presenting visual acuity of 6/18 or better in the better eye while 7% were blind with a visual acuity less than 3/60 according to the WHO classification of vision (Figure 2).

Figure 2: Presenting visual acuity among patients with haematological malignancies (N=99)

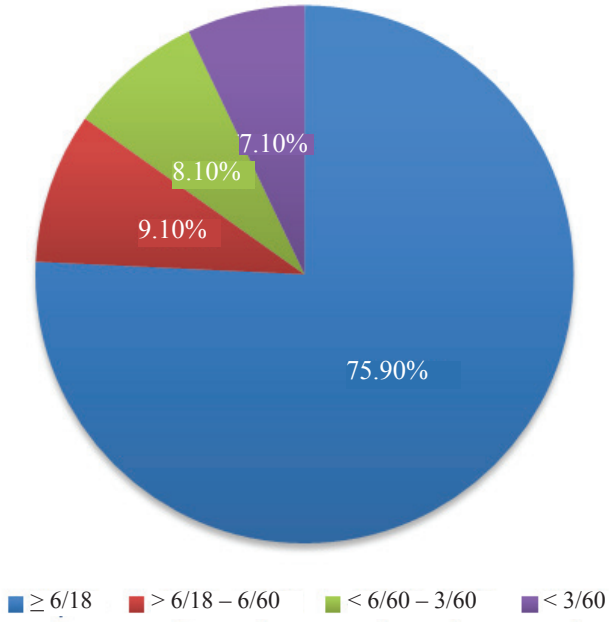


Table 3: Ocular manifestations among patients with haematological malignancies (N=99)

Group	Manifestations	No.	(%)
Ocular adnexa and anterior segment manifestations*	Proptosis	10	10.10
	Periorbital edema	14	14.10
	Ptosis	5	5.10
	Corneal ulcers	2	2.02
	Subconjunctival haemorrhage	21	21.20
	Chemosis	6	6.06
	Cells/Flare	2	2.02
	Pseudohypoyon	2	2.02
	Hyphema	2	2.02
	Iris nodule	1	1.01
Posterior segment*			
	Vitreous haemorrhage	4	4.04
	Optic nerve swelling	11	11.11
	Retinal infiltrates	15	15.15
	Subhyaloid haemorrhage	8	8.08
	Intraretinal haemorrhage	25	25.25
	Subretinal haemorrhage	3	3.03
	Roth spot	37	37.37
	Retinal detachment	2	2.02
	CRVO	3	3.03
	Cotton wool	9	9.09
	Optic atrophy	2	2.02

*Multiple responses for the variable, percentage do not add to hundred
CRVO=Central Retinal Vascular Occlusion

Ocular adnexa and anterior segment manifestation were present in 28.28%, where subconjunctival haemorrhage and periorbital edema were the most common features. Posterior segment manifestations were the commonest, present in 56.57% of patients. The frequently seen manifestations were the roth spots followed by intraretinal haemorrhage. Primary haematological malignancy infiltrates including optic nerve involvement and retinal infiltrates were present in 9.2% and 12.6% respectively (Table 3).

Table 4: Distribution of ophthalmic manifestations among patients with haematological malignancies at MNH and ORCI by demographic and clinical characteristics (N=99)

Characteristic	Ophthalmic manifestations			P-value
	Frequency			
		Yes	No	
	Total	No. (%)	No. (%)	
Sex				
Male	61 (61.6)	38 (62.3)	23 (37.7)	0.86
Female	38 (38.4)	23 (60.5)	15 (39.5)	
Age (years)				
≤17 (Paediatric)	35 (35.4)	19 (54.3)	16 (45.7)	0.267
18+ (Adults)	64 (64.6)	42 (65.6)	22 (34.4)	

AML_CML				
Yes	46 (46.5)	34 (73.9)	12 (26.1)	0.019
No	53 (53.5)	27 (50.9)	26 (49.1)	
MM				
Yes	14 (14.1)	8 (57.1)	6 (42.7)	0.71
No	85 (85.9)	53 (62.4)	32 (37.7)	
NHL				
Yes	11 (11.1)	4 (36.4)	7 (63.6)	0.099*
No	88 (88.9)	57 (64.8)	31 (35.2)	
HL				
Yes	2 (2.0)	0 (0)	2 (100)	0.145*
No	97 (98.0)	61 (62.9)	36 (37.1)	
WBC ($\times 10^9$/L)				
≤3	31 (31.3)	17 (54.8)	14 (45.2)	0.02
4-11	18 (18.2)	7 (38.9)	11 (61.1)	
>11	50 (50.1)	37 (74.0)	13 (26.0)	
PLT ($\times 10^9$/L)				
<150	67 (67.7)	45 (67.2)	22 (32.8)	0.186*
150-450	26 (26.3)	12 (46.2)	14 (53.9)	
>450	6 (6.1)	4 (66.7)	2 (33.3)	
RBC ($\times 10^{12}$/L)				
<4	73 (73.7)	50 (68.5)	23 (31.5)	0.018
4-6	26 (26.3)	11 (42.3)	15 (57.7)	
HB (g/dl)				
≤8	66 (66.7)	53 (80.3)	13 (19.7)	<0.001*
8.1-11	23 (23.2)	5 (21.7)	18 (78.3)	
>11	10 (10.1)	3 (30.0)	7 (70.0)	

**p-value from Fisher's exact test*

AML=Acute Myeloid Leukemia, ALL=Acute Lymphoblastic Leukemia, CML=Chronic Myeloid Leukemia, HL=Hodgkin Lymphoma. NHL=Non-Hodgkin Lymphoma. MM= Multiple Myeloma

The proportion of ophthalmic manifestations among patients with haematological malignancies at MNH and ORCI was 61.62%. Manifestations were more common among males, patients with myeloid leukemia, leukocytosis and low haemoglobin levels. (Table 4).

Table 5: Logistic regression analysis to assess factors associated with ophthalmic manifestations in patients with haematological malignancies at MNH and ORCI (N=99)

Characteristic	Ophthalmic manifestations		Crude OR (95%CI)	P-value	Adjusted OR (95% CI)	P-value
	Total	Yes				
Sex						
Male	61 (61.6)	38 (62.3)	1.03 (0.74-1.42)	0.86	1.07 (0.80-1.42)	0.64
Female	38 (38.4)	23 (60.5)	Ref		Ref	
Age (years)						
≤17 (Paediatric)	35 (35.4)	19 (54.3)	Ref		Ref	

18+ (Adults)	64 (64.6)	42 (65.6)	1.21 (0.85-1.72)	0.29	1.02 (0.73-1.43)	0.91
Level of education						
None/ Primary	20 (31.3)	15 (75.0)	1.39 (0.79-2.46)	0.25	-	
Secondary	13 (20.3)	7 (53.9)	Ref			
College	31 (48.4)	20 (64.5)	1.20 (0.68-2.12)	0.54	-	
Occupation						
Employed	32 (32.3)	22 (68.8)	1.25 (0.87-1.80)	0.22	-	
Self-employed	25 (25.3)	16 (64.0)	1.17 (0.78-1.75)	0.45		
No job	42 (42.4)	23 (54.8)	Ref			
Acute leukemia						
Yes	33 (33.3)	26 (78.8)	1.49 (1.11-1.98)	0.01	1.05 (0.76-1.44)	0.77
No	66 (66.7)	35 (53.0)	Ref		Ref	
MM						
Yes	23 (23.2)	15 (65.2)	1.08 (0.76-1.53)	0.68		
No	76 (76.8)	46 (60.5)	Ref		-	
NHL						
Yes	26 (26.3)	9 (34.6)	Ref		Ref	
No	73 (73.7)	52 (71.2)	2.06 (1.19-3.57)	0.01	1.42 (0.81-2.50)	0.22
HL						
Yes	2 (2.0)	0 (0)	IND			
No	97 (98.0)	61 (62.9)				
WBC ($\times 10^9$/L)						
0-3	31 (31.3)	17 (54.8)	1.41 (0.73-2.74)	0.31	Ref	
4-11	18 (18.2)	7 (38.9)	Ref		1.47 (0.82-2.66)	0.20
>11	50 (50.1)	37 (74.0)	1.90 (1.04-3.48)	0.04	1.19 (0.69-2.06)	0.54
PLT ($\times 10^9$/L)						
<150	67 (67.7)	45 (67.2)	1.46 (0.93-2.28)	0.10	1.05 (0.69-1.61)	0.81
150-450	26 (26.3)	12 (46.2)	Ref		Ref	
>450	6 (6.1)	4 (66.7)	1.44 (0.71-2.92)	0.31	1.72 (0.89-3.32)	0.11
RBC ($\times 10^{12}$/L)						
<4	73 (73.7)	50 (68.5)	1.62 (1.01-2.61)	0.05	Ref	
4-6	26 (26.3)	11 (42.3)	Ref		1.22 (0.76-1.96)	0.41
HB (g/dl)						
≤8	66 (66.7)	53 (80.3)	2.68 (1.03-6.98)	0.04	3.18 (1.08-9.36)	**0.04**
8.1-11	23 (23.2)	5 (21.7)	0.72 (0.21-2.48)	0.61	0.84 (0.23-3.10)	0.80
>11	10 (10.1)	3 (30.0)	Ref		Ref	

Note: All associations with p-value<0.20 in bivariate analysis plus age and sex were considered in multivariable analysis IND=Indeterminate; AML=Acute Myeloid Leukemia; ALL=Acute Lymphoblastic Leukemia; CML=Chronic Myeloid Leukemia; HL=Hodgkin Lymphoma' NHL=Non-Hodgkin Lymphoma; MM= Multiple Myeloma

In multivariate analysis, only haemoglobin level remained as an independent associated factor for the development of ophthalmological manifestation of haematological malignancy. Patients with haemoglobin levels of less than 8g/dl had 3.18 times increased odds (95%: 1.08-9.36) of having ophthalmic manifestation (Table 4).

DISCUSSION

This study focused on the prevalence, clinical presentation, and factors associated with haematological malignancies at two tertiary hospitals in urban Tanzania.

The prevalence of ocular manifestations of haematological malignancy in this study was high, relatively similar to the study done by Ilo *et al* in Nigeria[10]. The similarity to the findings of the Nigerian study may be accounted for by limited accessibility to haemato-oncological centers in Africa where patients usually seek health care services when the stages of disease are advanced with infiltration of different structures and significant haematological derangement that leads to ocular manifestations. The prevalence in this study was significantly higher than that found in India[11]. This may be accounted for by the availability of better health services and good health-seeking routine which aid early diagnosis of the disease before having ocular manifestation.

Visual impairment which is defined by visual acuity worse than 6/18 in the better eye according to WHO was present in nearly a quarter of the participants at (24.1%). This was higher than in a study carried out in India which found a (13.7%) prevalence[11]. This difference is because the Indian study included both newly diagnosed patients as well as patients who were already on treatment, unlike this study which included only newly diagnosed patients who had not started treatment. Treatment for the malignancies may cure some ocular manifestations leading to them not being identified during examination of the patients[11]. Vision threatening manifestations like optic nerve involvement, vitreous haemorrhage, retinal detachment and retinal vein occlusion were present in some participants in this study.

The most frequent anterior segment manifestation was subconjunctival haemorrhage. These results were similar to the findings in the study done by Eze *et al*[9] in Nigeria. The occurrence of subconjunctival haemorrhage may be attributed to low platelet count which causes coagulation dysfunction, hence leading into haemorrhage. Two-thirds of the participants in this study had a platelet count of less than 150×10^9/L, which puts them at a high risk for subconjunctival haemorrhage. Subconjunctival haemorrhage poses a psychological concern to the patients and its presence calls for a thorough evaluation of the underlying condition.

Posterior segment manifestations occurred more frequently than anterior segment features, with roth spots and intraretinal haemorrhage as the most common findings. This is similar to the findings in the study done by Renu *et al*[11] in India. The similarity may be due to the haematological cellular derangement in which damage of the blood vessels that leads into increased permeability and haemorrhages resulting into platelet aggregation causing roth spots. The presence of intraretinal haemorrhage may be sight-threatening depending on the location and severity. Follow-up is required as the observation of posterior segment manifestations may help in monitoring response to treatment because direct visualization of the malignant infiltration is possible during ocular examination.

Sight-threatening manifestations of retinal infiltrate and optic nerve involvement were present in a few of patients, (15.15%)[12]. This proportion was higher than that reported by Soman and Koshy in India[13,14]. The difference may be due to participants' late presentation to the hospital with infiltration of ocular structures in the current study. However, the Indian study also included patients who were already on treatment whose infiltration may have resolved by the time of ocular assessment. Chorio-retinal and optic nerve malignant infiltrates are observed in the end-stage of the disease and when the central nervous system is involved hence predicting a poor prognosis[12.15].

Haemoglobin levels of less than or equal to 8g/dl were the statistically significant factors associated with the presence of ocular manifestations. This was similar to the findings in the studies by Soman and Renu in India, where a low haemoglobin level of less than (7.35g/dl) was significantly associated with the occurrence of ocular manifestations[11,13]. A low level of haemoglobin leads to retinal hypoxia resulting in vascular dilatation, edema and haemorrhages. Low platelet counts further worsens the anaemia due to poor coagulation and haemorrhage. Early blood transfusion may be paramount to altering the pathogenesis[16].

Limitations

The study was limited by small sample size due to its relatively uncommon occurrence per year, a longer duration study needs to be done to get a bigger sample size. Being a hospital-based study may also limit generalization to the general population who have not come to the hospital.

CONCLUSIONS AND RECOMMENDATIONS

The proportion of ocular manifestations of haematological malignancies at MNH and ORCI is significantly high. Posterior segment manifestations were more frequent than anterior segment manifestations with intraretinal haemorrhage and roth spots as the most common manifestations. Sight-threatening complications such as sub-hyaloid haemorrhage retinal detachment, optic nerve swelling and optic atrophy were present in some patients. Lower level of haemoglobin increases the odds of occurrence of ophthalmic manifestations of haematological malignancies.

A comprehensive ophthalmic examination needs to be included in the evaluation protocol of patients with haematological malignancies for early detection and management of sight-threatening manifestations. More follow up studies need to be done to track the changes

with patients on treatment and to assess its association with patients' survival.

ACKNOWLEDGMENT

We thank all the mothers who consented their babies to be participants of this study. We thank the University of Dodoma for financial support. Muhimbili National Hospital and Ocean Road Cancer Institute for permission to collect data.

Declaration

Funding: Funded by The University of Dodoma.

Consent for publication: All the authors provided consent to submission of the manuscript

Availability of data and materials: The original full article is present from the author and at Muhimbili University Library. Any data needed is available from the corresponding author.

Authors' contributions: Gomba S designed the study, collected data, and analyzed through Statistical Package for Social Sciences (SPSS), also results interpretation, report writing and manuscript writing. Professor Mafwiri M, Nyamita O, Mhina C, Mosenene S and Sandi F were involved in proposal writing, data collection, and report writing. Further reviewed this manuscript for publication.

Competing interests: The authors declare no conflict of interest.

REFERENCES

1. Leak SA, Mmbaga LG, Mkwizu EW, *et al*. Hematological malignancies in East Africa. Which cancers to expect and how to provide services. *PLoS One* [Internet]. 2020;**15**(5):1–12. Available from: http://dx.doi.org/10.1371/journal.pone.0232848
2. Enawgaw B, Aynalem M, Melku M. Hematological malignancies in Northwest Ethiopia. *PLoS One*. 2021; **16**(12): e0260639
3. Mohan H. Textbook of Pathology, 6th edition, Jaypee brothers medical publisher. 2010.
4. Okello CD, Niyonzima N, Ferraresso M, *et al*. Haematological malignancies in sub-Saharan Africa: East Africa as an example for improving care. *The Lancet Haematol.* 2021; **8**(10):e756–e769.
5. Ohkoshi K, Tsiaras WG. Prognostic importance of ophthalmic manifestations in childhood leukemia. *Br J Ophthalmol*. 1992; **76**(11):651–655.
6. Japesh T, Anita M, Priyanka S, Panigrahi, Kumar P. Ophthalmic manifestations in hematological malignancies: An observational study from a tertiary care health center in Eastern India. *Indian J Ophthalmol.* 2024; **72**(5):659-663.
7. Charif Chefchaouni M, Belmekki M, Hajji Z, *et al*. Ophthalmic manifestations of acute leukemia. *J Fr Ophthalmol*. 2002; **25**(1):62–66.
8. Sharma T, Grewal J, Gupta S, *et al.* Ophthalmic manifestations of acute leukemias: The ophthalmologist's role. Vol. 18, Eye. Nature Publishing Group; 2004. p. 663–672.
9. 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.
10. Ilo OT, Adenekan AO, Alabi AS, *et al*. Ocular manifestations of leukemia: a teaching hospital experience. *Niger Postgrad Med J*. 2019; **26**: 205-210.
11. Dhasma R, Prakash A, Gupta N, *et al.* Ocular manifestations in leukemia and myeloproliferative disorders and their association with hematological parameters. *Ann Afr Med*. 2016; **15**(3): 97-103
12. Russo V, Scott I, Querques G, *et al.* Orbital and ocular manifestations of acute childhood leukemia: clinical and statistical analysis of 180 patients. *Eur J Ophthalmol.* 2008;**18**(4):619-623.
13. Soman S, Kasturi N, Srinivasan R, *et al*. Ocular manifestations in leukemias and their correlation with hematologic parameters at a tertiary care setting in South India. *Ophthalmol Retin*. 2018; **2**(1):17–23.
14. Koshy J, Joseph JM, Satish T, Kaur G. Ophthalmic manifestations of acute and chronic leukemias presenting to a tertiary care center in India. *Indian J Ophthalmol.* 2015; **63**(8): 659-664.
15. Abu el-Asrar AM. Correlation of fundus lesions and hematological findings in leukemic retinopathy. *Eur J Ophthalmol.* 1996; **6**(2): 167-172
16. Shah GY, Modi R. Anemic retinopathy: case reports and disease features. *Retina Today*. 2016; 30-32.