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Ocular morbidity among adult patients with chronic leukemia presenting to tertiary hospitals in Jos, North-Central Nigeria

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Background
Chronic leukemia is the most common leukemia subtype seen among adults in Jos, Nigeria, with few reported isolated cases of ocular morbidity. There are no published comprehensive data on adult leukemic ophthalmopathy from this region.
Aim
The aim of this study was to determine the prevalence, pattern, and causes of visual impairment (VI) among adult patients with chronic leukemia in Jos, North-Central Nigeria.
Patients and methods
The study included adult patients diagnosed with either chronic myeloid leukemia or chronic lymphocytic leukemia, confirmed by bone marrow biopsy, in two tertiary hospitals in Jos, North-Central Nigeria, between January 2016 and June 2017. Visual acuity was assessed and categorized using the International Classification of Diseases. Detailed ocular examination was carried out and causes of vision loss were noted.
Results
A total of 104 eyes of 52 patients were examined within the study period. The mean age of the patients was 45±17.7 years, and 35 (67.3%) patients were males. The majority (63.4%) of the participants had chronic myeloid leukemia. Ocular disorders were present in 32 (61.5%) of all patients, and 10 (19.2%) patients were visually impaired. Of these, nine (90.0%) had moderate VI due to refractive errors, cataract, glaucoma, and disk swelling; and one (10.0%) person was bilaterally blind from exudative retinal detachment and vitreous hemorrhage. Only 27% of all causes of VI were leukemia specific and included disk swelling, exudative retinal detachment, and vitreous hemorrhage.
Conclusion
Although ocular disorders were frequent among adults with chronic leukemia in Jos, the magnitude of vision loss from chronic leukemia-specific ocular disorders was low.

Keywords:
blindness, chronic leukemia, visual impairment

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Introduction

Chronic leukemia is the most common subtype among adult patients in Southern Nigeria with varying patterns of ocular involvement and vision loss identified [1–3]. Although chronic leukemia is a significant contributor to the leukemic pool in Jos, North-Central Nigeria, only few isolated cases of ocular morbidity have been reported [4–7]. Hence, the prevalence, pattern, and causes of vision loss among adult patients with chronic leukemia from this region remain unknown. Therefore, this study was undertaken to provide comparative data and to assist clinicians involved in the care of leukemia patients from this region to enhance their outcomes.

Patients and methods

This is a descriptive, hospital-based study that included newly diagnosed and known adult (≥18 years) leukemia patients, irrespective of treatment status, presenting to the hematology and blood transfusion units of two major referral hospitals in Jos, namely, the Jos University Teaching Hospital (JUTH) and the Bingham University Teaching Hospital (BHUTH), between January 2016 and June 2017 (18 months). The diagnosis of leukemia was made by bone marrow biopsy.

Patients were consecutively recruited for the study after signing a written informed consent to participate in the study and for publication of data. Those who did not consent or were unwilling to have a complete eye examination including dilated ophthalmoscopy or

moribund patients who were unable to have full ocular examination were excluded from the study. Ethical approval was obtained from the Health Research Ethics Committees of both hospitals, with reference numbers: JUTH/DCS/ADM/127/XIX/6062 (approved on March 16, 2015) and NHREC/21/05/2005/00148 (approved on August 20, 2015) for JUTH and BHUTH, respectively. The tenets of the Declaration of Helsinki for research involving human patients were upheld.

The patients were interviewed to obtain their sociodemographic and medical history. Visual acuity (VA) was measured by an ophthalmic nurse with available correction at a distance of 3 m using an illuminated reverse Snellen's chart in front of a '24×18' mirror to obtain the presenting visual acuity (PVA). Refraction was performed by the optometrist for patients with PVA worse than 6/18 to obtain the best-corrected VA. Each eye was tested separately, with the right eye being tested first in all instances. Both eyes were then tested together for PVA and best-corrected VA in person. Ocular examination included that of the ocular adnexa with a pen torch, slit-lamp examination of the anterior segment, direct and indirect ophthalmoscopy of the posterior segment including dilated fundoscopy. Mydriatic fundus photographs were taken for patients with significant fundus pathology using a Canon CR-2 digital retinal camera (Canon Inc., Medical Equipment Group, 30–2, Shimomaruko 3-chrome, Ohta-ku, Tokyo, Japan).

Study definitions

(1) International Classification of diseases-10 definition of visual impairment (VI)/blindness [8].
   (a) Normal vision: PVA more than or equal to 6/18 in the better eye.
   (b) Moderate visual impairment (MVI) : less than 6/18–6/60 in the better eye.
   (c) Severe VI: PVA less than 6/60–3/60 in the better eye.
   (d) Blindness: PVA less than 3/60 in the better eye.
(2) Adult: a person aged 18 years and above.
(3) Ocular abnormalities were classified as follows [9]:
   (a) Primary ocular complications: likely to result from leukemic infiltrates. They included proptosis, iris heterochromia, retinal leukemic infiltrates, and Roth spots.
   (b) Secondary ocular complications: likely to result from systemic therapy or hematological alterations such as anemia, thrombocytopenia, hyperviscosity, or immune deficiency. They included retinal hemorrhages, vascular abnormalities, disk swelling, and vitreous hemorrhage (VH).
   (c) Miscellaneous ocular abnormalities: eye diseases unlikely to be related to leukemia such as pterygium, cataract, pseudophakia, and glaucoma.

Statistical analysis

The collected data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 21 (IBM SPSS Statistics for Windows, version 21.0; IBM, Armonk, New York, USA). Frequency distribution tables were generated for all data collected. Fisher's exact test was used to test the association between some categorical variables. A *P* value of less than 0.05 was considered statistically significant.

Results

A total of 52 adults with chronic leukemia managed in the two tertiary hospitals during the study duration were enrolled. The age of the study participants ranged between 18 and 78 years (mean=45±17.7 years). The male to female ratio was 2.1 : 1. Twenty-seven (51.9%) patients were newly diagnosed, and 17 (32.7%) patients had ocular complaints at the time of eye examination, which were mainly impairment in the distant vision (15 patients) and ocular pain (two patients) (Table 1).

A total of 104 eyes of 52 patients were evaluated for ocular morbidity. Ocular manifestations were detected in 32 (61.5%) of them. More than half 17 (53.1%) of those with ocular manifestations had chronic myeloid leukemia (CML). The distribution of ocular manifestation by leukemia subtype was not found to be statistically significant (P=0.05). The ocular findings in patients with chronic lymphocytic leukemia (CLL) were predominately miscellaneous, while those in CML patients were largely from secondary causes, which was statistically significant (P<0.001, Table 2).

VI was found in 10 (19.2%) patients, nine (17.3%) of them had MVI, while one (1.9%) patient was bilaterally blind. After refraction, one patient remained bilaterally blind from exudative retinal detachment (ERD) (Fig. 1) and VH, while five (4.8%) patients remained with MVI. Unilateral MVI was found in 18 (17.3%) eyes, which was reduced to 10 (9.6%) post-refraction, while the proportion of unilateral blind eyes (five, 4.8%) did not change after

refraction (Table 3). The pattern of refractive error was myopia in 10 eyes, hypermetropia in two eyes, and astigmatism in one eye. Other causes of VI among the study population were cataract, glaucoma, and disk swelling (Fig. 2). The distribution of ocular changes among the study population is shown in Table 4.

Potentially blinding disorders such as maculopathy, retinal hemorrhage, and disk swelling were detected among the study population. Only 27.3% (3/11) of the causes of vision loss were leukemia specific and included disk swelling, ERD, and VH, while the remaining were from miscellaneous causes (Fig. 3).

Table 1 Summary statistics of the study population

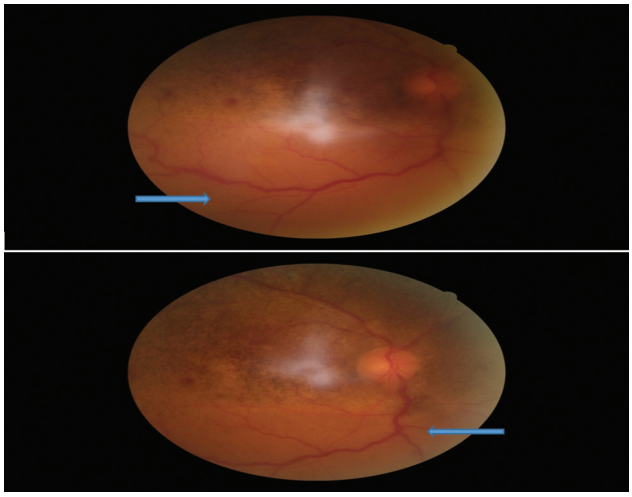
Characteristic of participants (*N*=52)	*n* (%)
Age groups (years)	
≤20	2 (3.8)
21–30	14 (26.9)
31–40	9 (17.3)
41–50	4 (7.7)
51–60	10 (19.2)
61–70	7 (13.5)
>70	6 (11.5)
Sex	
Male	35 (67.3)
Female	17 (32.7)
Type of leukemia	
CLL	19 (36.5)
CML	33 (63.5)
Ocular complaint at examination	
Present	17 (32.7)
Absent	35 (67.3)

CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia

Discussion

Leukemia is a malignant disorder of bone marrow leukopoietic stem cells, characterized by clonal proliferation and overcrowding of the bone marrow by immature or dysfunctional white blood cells. This

Figure 1



Fundus photograph of a 35-year-old patient with chronic myeloid leukemia showing inferior exudative retinal detachment (blue arrow).

Table 2 Distribution of ocular manifestation by leukemia subtype

Ocular manifestation	Type of leukemia [*n* (%)]			Fisher's exact
	CLL (*N*=19)	CML (*N*=33)	Total (*N*=52)	*P* value
Present	15 (78.9)	17 (51.5)	32 (61.5)	0.050
Absent	4 (21.1)	16 (48.5)	20 (38.5)	
Total	19 (100.0)	33 (100.0)	52 (100.0)	
Primary	0	3 (9.1)	3 (5.8)	
Secondary	2 (10.5)	8 (24.2)	10 (19.2)	<0.001*
Miscellaneous	13 (68.4)	6 (18.2)	19 (36.5)	
Absent	4 (21.1)	16 (48.5)	20 (38.5)	
Total	19 (100.0)	33 (100.0)	52 (100.0)	

CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia. *Statistically significant.

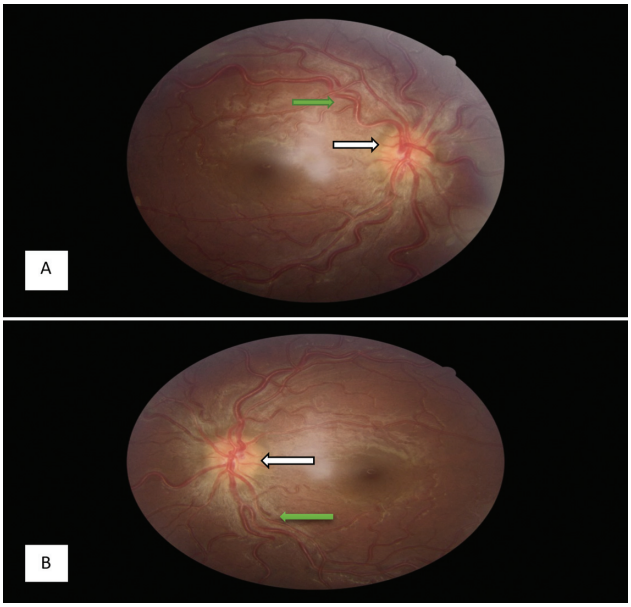
Table 3 Visual acuity distribution of study population in eyes and persons

Visual acuity category	PVA [*n* (%)]		BCVA	
	Eyes	Person	Eyes	Person
Normal vision (6/6–6/18)	81 (77.9)	42 (80.8)	89 (85.6)	46 (88.5)
Moderate visual impairment (<6/18–6/60)	18 (17.3)	9 (17.3)	10 (9.6)	5 (9.6)
Severe visual impairment (<6/60–3/60)	0	0	0	0
Blindness (<3/60)	5 (4.8)	1 (1.9)	5 (4.8)	1 (1.9)
Total	104 (100.0)	52 (100.0)	104 (100.0)	52 (100.0)

BCVA, best-corrected visual acuity; PVA, presenting visual acuity.

results in spillage of these neoplastic white blood cells into the peripheral circulation, with widespread infiltration of tissues and organs [10,11]. Based on the origin of the precursor cells, leukemia could be either lymphoid or myeloid, acute or chronic depending on the clinical course [11]. Hence, using both the cell lineage and clinical course of the diseases, chronic leukemia can be classified as CML or CLL [10,11]. Although all forms of leukemia can affect patients at any age, most cases of chronic leukemia occur in adults [1–3,12].

Figure 2



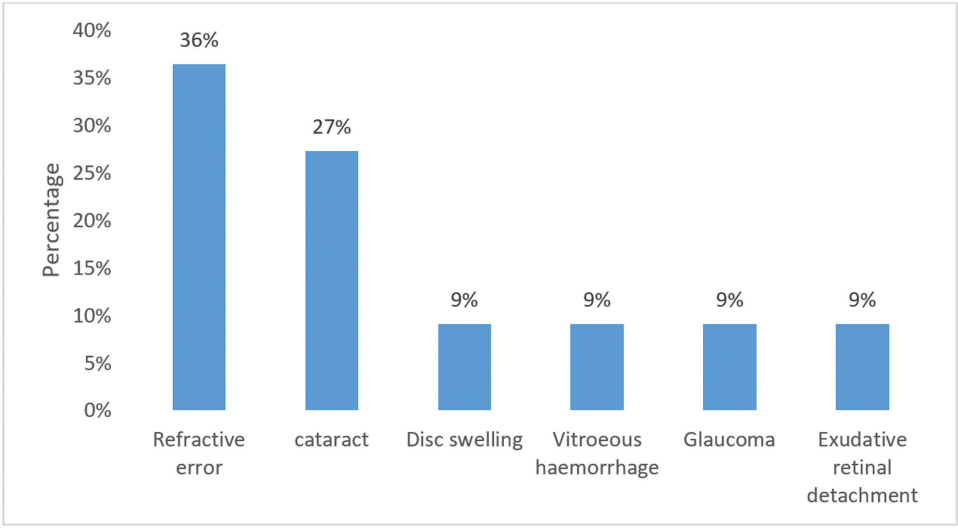
Fundus photograph of a 25-year-old patient with chronic myeloid leukemia showing disk swelling (white arrow) and tortuous retinal vessels (green arrow) in the right eye (a) and in the left eye (b).

Table 4 Ocular manifestations

Type of manifestation	Specific ocular manifestations	*n* (%)
Primary	Iris heterochromia	2 (1.4)
	Disk swelling[a]	7 (5.1)
	Retinal infiltrate	1 (0.7)
	Perivascular sheathing	1 (0.7)
	Roth spots	2 (1.4)
Secondary	Pallor	25 (18.1)
	CCSV	7 (5.1)
	Periorbital edema	5 (3.6)
	Chemosis	1 (0.7)
	Conjunctiva injection	2 (1.4)
	Jaundice	2 (1.4)
	Subconjunctiva hemorrhage	1 (0.7)
	Tortuous retinal vessels	12 (8.7)
	Retinal hemorrhage[a]	7 (5.1)
	Maculopathy[a]	8 (5.8)
	Cotton wool spots	5 (3.6)
	Disc hemorrhage[a]	1(0.7)
	Exudative retinal detachment[a]	1 (0.7)
	Vitreous hemorrhage[a]	1 (0.7)
Miscellaneous	Pingueculum	3 (2.2)
	Pterygium	3 (2.2)
	Cataract[a]	31 (22.5)
	Pseudophakia	3 (2.2)
	Glaucoma[a]	6 (4.3)
	Asteroid hyalosis	1 (0.7)
Total		138 (100)

CCSV, conjunctival corkscrew vessels. Some patients had two or more findings in two or more segments of both eyes. [a]Potentially blinding manifestation.

Figure 3



NB: one patient was bilaterally blind from Exudative retinal detachment and vitreous hemorrhage

Causes of visual impairment/blindness among 10 study participants.

Ocular involvement in leukemia results from either direct infiltration of the ocular tissues or indirectly, secondary to hematologic alterations such as anemia and thrombocytopenia with resultant VI in some instances [10,11]. Although ocular disorders associated with vision loss among adult leukemia patients from the southern parts of Nigeria have been well documented, comparative data from the northern region of the country are limited [1–3]. This study, therefore, provides the first comprehensive report on the prevalence, pattern, and causes of VI from the most common type of leukemia among adult patients in Jos, North-Central Nigeria.

The mean age of the patients of 45 years and the male preponderance in the current study population is in conformity with the distribution of leukemia among adult patients presenting to tertiary centers in Nigeria and other developing countries [1,3,13–15]. The observed male predominance may suggest a natural predilection for the male sex in the pattern of leukemia or a sex inequality in access and utilization of health-care services in developing settings, in which women are disadvantaged.

CML was the predominant subtype among our cohort with similar reports from previous studies from Nigeria [1–5,16]. This is in contrast with reports from the Western world, where CLL has been described as the most frequent subtype [17,18]. The disparity in distribution of leukemia subtypes might not be unrelated to genetic and geographical variations. The ophthalmic manifestations in CML have been described as more frequent and elaborate when compared with CLL which is a less aggressive variant with a more indolent course [2,3,9,17].

Most of the patients, in the present study, did not have ocular complaint at the time of presentation and most of them had normal vision, which is similar to previous studies from Nigeria [1–3]. The prevalence of VI of 19.2% among patients with chronic leukemia, in the present study, is much lower than the 33.8, 32.1, and 37.1% reported by Ilo *et al*. [2], Eze *et al*. [3], and Gawai *et al*. [15] in South-West, South-East Nigeria and India, respectively, who all studied adults with both acute and chronic leukemia with CML as the predominant subtype. However, it differs markedly from the 8.5% documented by Omoti *et al*. [1] in South-South Nigeria who had more patients with CLL. Similarly, Schachat *et al*. [19] whose patients largely had acute leukemia reported a prevalence of 5.0% in both children and adult patients in the United States. The authors did not come across a study that specifically looked at VI in adult patients with chronic leukemia alone. Nonetheless, the wide variation in the prevalence of VI might be attributable to differences in sample size, case mix, lack of standardization of VA assessment protocol, and variation in the threshold used for VI in various studies. Furthermore, in many resource-limited settings, late presentation with advanced disease can contribute significantly to the higher prevalence of VI, as late disease is more likely to be associated with more visually impairing ocular disorders. There is also the possibility that the prevalence of VI was underestimated in some surveys in which patients who were uncooperative or moribund were excluded from VA assessment even though potentially vision-impairing ocular disorders were reported to have been detected in most of them. Because all recruits in the current study underwent VA assessment using a standardized protocol and those moribund or unwilling to complete an eye examination were excluded from the survey, our estimates of the prevalence of VI is less likely to be inaccurate.

The majority of those who were visually impaired in the current study had MVI, while only one patient with CML was bilaterally blind from ERD and Ilo *et al*. [2] also reported a case of monocular blindness from ERD in a patient with CML. The causes of MVI in the present study included refractive errors, cataract, glaucoma, and disk swelling with only 20% of all causes of VI being leukemia specific. Previous surveys from Nigeria had reported a wider variety of vision-impairing disorders such as proptosis, cataract, retinopathy, age-related macular degeneration, optic atrophy, maculopathy, and VH as the main causes of VI among their study participants [1,3]. In addition, some authors from Malaysia and the United States found that VH, central retinal vein occlusion, ERD, and cortical blindness were responsible for vision loss in their patients [13,19]. The small sample size in the present study might had limited the spectrum of vision-impairing ocular manifestations detected. It is worth noting that some of the aforementioned studies might have had more varieties of vision-impairing disorders due to a larger sample size, wider case mix, or longer study duration when compared with the current survey. Some causes of vision loss such as refractive error, cataract, and glaucoma detected in this study and other similar studies are thought to be coexisting ocular morbidities as they are not known to be directly related to hematologic malignancy. However, their detection underscores the importance of comprehensive ocular assessment for patients with leukemia. Therefore, it is important to consider an ophthalmic assessment at diagnosis and periodically

during the course of treatment to prevent vision loss and to optimize vision.

Conclusion

Ocular disorders occur in adult patients with chronic leukemia in Jos, Nigeria, some of which are potentially blinding. An interdisciplinary approach involving the ophthalmologist and hematologist is needed to promote early detection and to prompt treatment in order to avert vision loss and to improve the overall quality of life of leukemia survivors.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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