Original Article

HAEMATOLOGICAL RISK FACTORS ASSOCIATED WITH OCULAR FEATURES OF PATIENTS WITH LEUKAEMIA DISORDERS ATTENDING UNIVERSITY OF BENIN TEACHING HOSPITAL, NIGERIA.

[1]Obasi CU, [2]Omoti CE, [3]Ukponmwan CU, [4]Omoti AE

[1]Consultant Ophthalmologist, Department of Ophthalmology, FMC Abakaliki; [2]Prof/Consultant Haematologist, UBTH, Benin; [3,4]Prof/Consultant Ophthalmologist, UBTH, Benin City

ABSTRACT

Aim: To evaluate the risk factors for the development of ocular manifestations in patients with leukaemia in University of Benin Teaching Hospital, Nigeria.

Method: This is a hospital- based case control study from Sept 2014 to April 2015. Forty newly diagnosed patients with leukaemia were enrolled into the study. Age and sex matched controls were drawn from healthy relatives of patients, staff, and students of University of Benin and children of University of Benin Staff School. They had Full Blood Count, Genotype, Fasting blood sugar and other tests done to exclude confounding factors such as diabetes mellitus, HIV and hypertension. All the study subjects were interviewed with biodata. Detailed ocular examination were carried out including refraction where necessary. Clinical data from each individual was obtained using interviewer administered questionnaires. These were collated and analyzed using SPSS 20.

Results: There were forty naive patients (cases) with leukaemia and forty controls. The eye changes were seen more often in adults 22 eyes (35.5%) than in children 2 eyes (11.1%) and in myeloid leukaemia than in lymphoid leukaemia. There was a significant relationship between thrombocytopenia and subconjunctival and intraretinal haemorrhage (OR=4.840, 5.056; p=0.014 and 0.008 respectively). Leucocytosis and proptosis, retinal infiltrates, neovascularization, microaneurysm, venous dilatation also had statistically significant relationships (OR=3.016, 3.704, 3.016, 3.016, 3.704; p = 0.041, 0.022, 0.041, 0.041, 0.022 respectively). Anaemia had a statistically significant association with conjunctival pallor (OR=27.279; p =0.001). Patients with leukaemia were more likely to develop hypermetropia (p=0.000).

Conclusion: Age, thrombocytopenia, anaemia and high WBC count were the risk factors identified in the development of ocular manifestation in leukaemia patients.

Key words: risk factors, leukaemia, ocular

INTRODUCTION

Ocular involvement with leukaemia is common, occurring in as many as 80% of the eyes of patients examined at autopsy.[1] Ocular features are due to infiltration of the eyeball, orbital tissues and ocular adnexa. They also occur due to bone marrow failure, central nervous system involvement, and occurrence of opportunistic infections.[1] Bone marrow failure – anaemia (pallor, lethargy and dyspnoea), neutropenia (fever, malaise), and features of leukaemia may involve many ocular tissues either by direct infiltration, haemorrhage, ischaemia, or toxicity due to various chemotherapeutic agents.[2]

Leukaemic patients being managed by haematologists or oncologists may not be referred for ophthalmic examination; hence ocular manifestations may be missed.

All correspondence to:
Prof Caroline E. Omoti MBBS, FMCPath,
Consultant Haematologist, UBTH, Benin City,
Nigeria. Email: caroline.omoti@uniben.edu

Furthermore, the doctors managing leukaemic patients may not routinely examine the eyes thereby increasing the possibilities for missed ocular manifestations**.**

The eye is a sanctuary site for leukaemia.[3] Thus, lesions within the eye may be missed if they are not carefully searched for. Such lesions may promote reoccurrence and relapse in patients that are being treated for leukaemia. Hence there is a need to have a closer look at the ocular manifestations in leukaemic patients as these can be life threatening. Some lesions that can occur in leukaemia can result in visual impairment and blindness. These include optic atrophy, retinal detachment, proptosis; these can reduce quality of life of these patients if not detected and properly managed.

Many patients with leukaemia in Nigeria present late.[4] It is possible that such patients may have a higher frequency and severity of the ocular manifestation compared to studies from advanced countries. This study is designed to identify risk factors for the development of ocular disorders in leukaemia.

TABLE 1: FREQUENCY OF LEUKAEMIC OCULAR DISORDERS AMONG THE EYES OF ALL CASES IN UBTH

Variables	Frequency	Percent (%)
Eyes of cases (n = 80)		
Present	24	30.0
Absent	56	70.0
Eyes of children (n = 18)		
Present	2	11.1
Absent	16	88.9
Eyes of adults (n = 62)		
Present	22	35.5
Absent	40	64.5

*This table takes note of each individual eye

MATERIALS AND METHODS

This is a prospective hospital based case control study conducted at Haematology clinic and ward, Paediatric clinic and wards; Ophthalmology clinic and ward in the University of Benin Teaching Hospital (UBTH), Benin City, from September 2014 to April 2015. Ethical approval was obtained from the Ethics and Research Committee of the University of Benin Teaching Hospital (UBTH), Benin City, Nigeria.

Forty four patients with leukaemia were recruited and 4 were excluded based on the exclusive criteria. The remaining 40 patients were enrolled into the study having met the inclusion criteria. All the naive patients with leukaemia were interviewed for their bio data, and had clinical and laboratory evaluation including peripheral blood film and confirmation by bone marrow aspiration cytology, trephine biopsy mainly at the posterior segment of the bone marrow. All the study population had detailed ocular examination done along with refraction where necessary and the ocular finding recorded. Proper diagnosis of the type of leukaemia, ocular findings and identification of any existing co-morbidities was noted. The possible haematological risk factors and the ocular findings was noted with the patients Full Blood Count, Genotype and other tests done to exclude confounding factors such as diabetes mellitus, sickle cell retinopathy, HIV/AIDS. The haematological blood parameters were defined as follows: thrombocytopenia refers to a relative decrease of platelets in blood. (Normal platelet count ranges from 150,000 to 450,000 platelets/mm^3 of blood).[5] Leukocytosis refers to an increase in the total number of white blood cells above normal. (Normal white blood cell count is 4,000-11,000 cells/mm^3).[6] Anaemia was classified into three groups according to WHO guideline: mild, moderate and severe anaemia.[7] The control was drawn from healthy patient's relatives, staff and students of University of Benin and children of University of Benin Staff School. These were age and sex matched with the cases.Clinical data from each individual in the study was obtained using interviewer

administered questionnaires. This was statistically collated and analyzed with SPSS 20.

TABLE 2: POSTERIOR SEGMENT DISORDER IN THE EYES OF THE CASES AND CONTROLS IN UBTH

Disorder	Class			df	Fisher's exact test	p value
	Case n (%)	Control n (%)	Total n (%)			
Vitreous haemorrhage	1 (1.3)	0 (0.0)	1 (0.6)	1	1.006	0.999
**Disc oedema	1 (1.3)	0 (0.0)	1 (0.6)	1	1.006	0.999
**Optic atrophy	2 (2.5)	0 (0.0)	2 (1.3)	1	2.025	0.497
**Glaucoma	10 (12.5)	3 (3.8)	13 (8.1)	1	4.103	0.079
**Intraretinal haemorrhage	13 (16.3)	0 (0.0)	13 (8.1)	1	14.150[x]	0.000*
Retinal infiltrates	8 (10.0)	0 (0.0)	8 (5.0)	1	8.421	0.007*
Neovascularization	7 (8.8)	0 (0.0)	8 (4.4)	1	7.320	0.014*
Microaneurysms	7 (8.8)	0 (0.0)	8 (4.4)	1	7.320	0.014*
Venous dilatation and tortuosity	8 (10.0)	0 (0.0)	8 (5.0)	1	8.421	0.007*
Roth spots	2 (2.5)	0 (0.0)	2 (1.3)	1	2.025	0.497
Perivascular sheathing	2 (2.5)	0 (0.0)	2 (1.3)	1	2.205	0.497
**Exudative RD	3 (3.8)	0 (0.0)	3 (1.9)	1	3.057	0.245
**Cystoid macula oedema	1 (1.3)	0 (0.0)	1 (0.6)	1	1.006	0.999
**ARMD	8 (10.0)	3 (3.8)	11 (6.9)	1	2.441	0.210
Cotton wool spots	4 (5.0)	0 (0.0)	4 (2.5)	1	4.103	0.120

***Significant** [x]**Pearson chi square**

****Potentially blinding complications**

cell disease). Age and sex has no significant relationship with anterior and posterior segment leukaemic disorders. Twenty four (30.0%) of the eyes of the cases had ocular disorders comprising of 2 (11.1%) eyes among the children and 22 (35.5%) eyes among the adults had these ocular disorders due to leukaemia (Table 1). There is thus an increased frequency of leukaemic disorders among adults compared to children.

RESULTS

A total of 160 eyes comprising of 80 subjects were examined within the study period. They comprised 23 (57.5%) males and 17 (42.5%) females with a male to female ratio of 1.35:1. Forty controls were recruited who were matched for age and sex after excluding confounders (diabetes mellitus, hypertension, HIV and sickle

The eye changes were seen more in adults 22 (35.5%) than in children 2 (11.1%) and in myeloid leukaemia than lymphoid leukaemia. Ocular

TABLE 3: ANTERIOR SEGMENT DISORDER IN THE EYES OF THE CASES AND CONTROLS IN UBTH

Disorders	Class			df	Fisher's exact test	p value
	Case n (%)	Control n (%)	Total n (%)			
**Proptosis	7 (8.8)	0 (0.0)	7 (4.4)	1	10.024	0.007*
Periorbital oedema	6 (7.5)	0 (0.0)	6 (3.8)	1	6.234	0.028*
Chalazion	2 (2.5)	0 (0.0)	2 (1.3)	1	2.025	0.497
Subconjunctival haemorrhage	12 (15.0)	0 (0.0)	12 (7.5)	1	12.973	0.000*
Conjunctival pallor	18 (22.5)	0 (0.0)	18 (11.3)	1	20.282[x]	0.000*
Pterygium	8 (10.0)	4 (5.0)	12 (7.5)	1	1.441[x]	0.369
Allergic conjunctivitis	20 (25.0)	14 (17.5)	34 (21.3)	1	1.345[x]	0.246
Corneal ulcer	0 (0.0)	0 (0.0)	0 (0.0)			
Spontaneous hyphaema	1 (1.3)	0 (0.0)	1 (0.6)	1	1.006	0.999
Iris nodule	1 (1.3)	0 (0.0)	1 (0.6)	1	1.006	0.999
**Cataract	20 (25.0)	18 (22.5)	38 (23.8)	1	0.138[x]	0.710

***Significant** [x]**Pearson chi square** ****Potentially blinding complications**

leukaemic disorders were present in 12 (30.0%) patients. Visual loss occurred in 8 eyes (10%) of cases and of the 4 mortalities, 2 (50.0%) were AML patients, while the other two had CLL and CML. Table 2 shows significant increased tendency to have intraretinal haemorrhage among cases compared to control (p = 0.000). This tendency was also present in retinal infiltrates, neovascularization, microaneurysms and venous dilatation and tortuosity (p = 0.007, 0.014, 0.014 and 0.007 respectively). Table 3 showed significantly increased tendency to have proptosis, periorbital oedema, subconjunctival haemorrhage and conjunctival pallor among the cases compared to the control group (p = 0.007, 0.028, 0.000 and 0.000 respectively).

There was significant relationship between thrombocytopenia and subconjunctival haemorrhage, intraretinal haemorrhage (p=0.014 and 0.008 respectively). Table 4 shows that, there was an increased tendency for cases with platelet counts less than 150000 to have subconjunctival haemorrhage compared to those with platelet counts >150000. This finding was statistically significant (p = 0.014). Majority, 28 (70.0%) of the cases had increased tendency for low platelet counts while 12 (30.0%) had normal platelet count. There was an increased tendency for cases with platelet counts less than 150000 to have intraretinal haemorrhage compared to those with platelet counts >150000. This finding was statistically significant (p = 0.008). There were 13 cases (23%) with intraretinal haemorrhages with platelet count less than 150,000/mm^3 and no case with intraretinal haemorrhage with platelet count 150,000 – 450,000/mm^3 (OR= 5.056, Fishers exact test = 6.652, p= 0.008). None of the posterior segment disorders had a significant relationship with the age and sex of the cases and controls.

There was an increased tendency for cases with white blood cell counts >11000/mm^3 to have retinal infiltrates, neovascularization, microaneurysms and venous dilatation compared to those with WBC counts < 11000/mm^3 (Table 5). This finding was statistically significant (p = 0.022, 0.041, 0.041 and 0.022 respectively). Nearly two thirds 25 (62.5%) of the cases had very high (20,000/mm^3) white blood cell counts while 15 (37.5%) of the cases had high WBC counts. The

TABLE 4: ASSOCIATION BETWEEN PLATELET COUNT AND ANTERIOR SEGMENT DISORDER IN THE EYES OF THE CASES AND CONTROLS IN UBTH

Disorder		Platelet count			df	Fisher's exact test	Pvalue
		<150000 n (%)	150000 – 450000 n (%)	Total n (%)			
Proptosis	Case	7 (12.5)	0 (0.0)	7 (8.8)	1	3.288	0.096
	Control	0 (0.0)	0 (0.0)	0 (0.0)			
Periorbital oedema	Case	4 (7.1)	2 (8.3)	6 (7.5)	1	0.034	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)			
Chalazion	Case	2 (3.6)	0 (0.0)	2 (2.5)	1	0.879	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)			
Subconjunctival haemorrhage	Case	12 (21.4)	0 (0.0)	12 (15.0)	1	6.050	0.014*
	Control	0 (0.0)	0 (0.0)	0 (0.0)			
Conjunctival pallor	Case	10 (17.9)	8 (33.3)	18 (22.5)	1	2.308	0.151
	Control	0 (0.0)	2 (2.5)	2 (2.5)			
Pterygium	Case	4 (7.1)	4 (16.7)	8 (10.0)	1	1.693	0.232
	Control	0 (0.0)	4 (5.0)	4 (5.0)			
Allergic conjunctivitis	Case	12 (21.4)	8 (33.3)	20 (25.0)	1	1.270	0.273
	Control	0 (0.0)	14 (17.5)	14 (17.5)			
Corneal ulcer	Case	0 (0.0)	0 (0.0)	0 (0.0)			
	Control	0 (0.0)	0 (0.0)	0 (0.0)			
Spontaneous hyphaema	Case	1 (1.8)	0 (0.0)	1 (1.3)	1	0.434	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)			
Iris nodule	Case	0 (0.0)	1 (4.2)	1 (1.3)	1	2.363	0.300
	Control	0 (0.0)	0 (0.0)	0 (0.0)			
Cataract	Case	14 (25.0)	6 (25.0)	20 (25.0)	1	0.000	0.999
	Control	0 (0.0)	18 (22.5)	18 (22.5)			

***Significant**

cases with white blood cell counts > 11000/mm^3 had an increased tendency to have proptosis compared to those with WBC counts < 11000/mm^3. Seven cases of proptosis (14%) occurred in cases with white blood cell count greater than 20,000/mm^3, but no cases of proptosis occurred in leukaemia patients with white blood cell count less than 20,000/mm^3. This finding was statistically significant (OR=3.016, Fishers exact test=4.603, p = 0.041). There was a significant increased tendency for adult cases with white blood cell counts > 11000/mm^3 to have conjunctival pallor compared to those with WBC counts < 11000/mm^3 (p = 0.009). Ten cases of patients with leukaemia (45.5%) had white blood cell count greater than 11,000/mm^3 and 6 cases (15.0%) had white blood cell count greater than 20,000/mm^3 but no case had white blood cell count less than or equal to 11,000/mm^3 (OR= 5.377, Fishers exact test = 6.875 and p= 0.009). None of the anterior segment disorders had a significant relationship with the WBC count of the children cases and controls.

There was significant relationship between anaemia and conjunctival pallor (p =0.001). The highest proportion 17 (42.5%) of the cases had mild anaemia while 3 (7.5%) had normal packed cell volume. There was an increased tendency for adult cases with anaemia to have conjunctival

TABLE 5: ASSOCIATION BETWEEN WHITE BLOOD CELL COUNT AND POSTERIOR SEGMENT DISORDER IN THE EYES OF THE CASES AND CONTROLS IN UBTH

Disorder		White blood cell count				OR	Fisher's exact test	p value
		≤ 11,000 n (%)	>11,000 - 20,000 n (%)	> 20,000 n (%)	Total n (%)			
Vitreous haemorrhage	Case	0 (0.0)	0 (0.0)	1 (2.0)	1 (1.3)	0.000	0.608	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Disc oedema	Case	0 (0.0)	0 (0.0)	1 (2.0)	1 (1.3)	0.000	0.608	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Optic atrophy	Case	0 (0.0)	0 (0.0)	2 (4.0)	2 (2.5)	0.137	1.231	0.525
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Glaucoma	Case	0 (0.0)	2 (6.7)	8 (16.0)	10 (12.5)	0.762	1.493	0.306
	Control	4 (5.0)	0 (0.0)	0 (0.0)	4 (5.0)			
Retinal infiltrates	Case	0 (0.0)	0 (0.0)	8 (16.0)	8 (10.0)	3.704	5.333	0.022*
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Intraretinal haemorrhage	Case	0 (0.0)	2 (6.7)	11 (22.0)	13 (16.3)	2.210	3.239	0.116
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Neovascularization	Case	0 (0.0)	0 (0.0)	7 (14.0)	7 (8.8)	3.016	4.603	0.041*
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Microaneurysms	Case	0 (0.0)	0 (0.0)	7 (14.0)	7 (8.8)	3.016	4.603	0.041*
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Venous dilatation	Case	0 (0.0)	0 (0.0)	8 (16.0)	8 (10.0)	3.704	5.333	0.022*
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Roths spots	Case	0 (0.0)	0 (0.0)	2 (4.0)	2 (2.5)	0.137	1.231	0.525
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Perivascular sheathing	Case	0 (0.0)	0 (0.0)	2 (4.0)	2 (2.5)	0.137	1.231	0.525
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Exudative RD	Case	0 (0.0)	0 (0.0)	3 (6.0)	3 (3.8)	0.577	1.870	0.288
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Cystoid macula oedema	Case	0 (0.0)	0 (0.0)	1 (2.0)	1 (1.3)	0.000	0.608	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Cotton wool spots	Case	0 (0.0)	1 (3.3)	3 (6.0)	4 (5.0)	0.000	0.281	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
ARMD	Case	0 (0.0)	2 (6.7)	6 (12.0)	8 (10.0)	0.148	0.593	0.703
	Control	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)			

***Significant** **OR- Odds ratio**

pallor compared to those with normal PCV (Table 6). This finding was statistically significant (p = 0.000). Cataract was significantly more common in patients with anaemia than those without anaemia (p=0.003). There was an increased tendency for children cases with anaemia to have proptosis, subconjunctival haemorrhage and conjunctival pallor compared to those with normal PCV. These findings were statistically significant (OR= 18.000, p = 0.007 each).

Thirty three (82.5%) of the cases had genotype AA while 7 (17.5%) had AS. There was a significant relationship between genotype and pterygium in

TABLE 6: ASSOCIATION BETWEEN PACKED CELL VOLUME AND ANTERIOR SEGMENT DISORDER IN THE EYES OF THE ADULTS IN UBTH

Disorders		Packed cell volume					OR	Fisher's exact test	p value
		Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Total n (%)			
Proptosis	Case	0 (0.0)	3 (12.5)	1 (3.8)	1 (16.7)	5 (8.1)	0.929	2.386	0.450
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Periorbital oedema	Case	0 (0.0)	2 (8.3)	4 (15.4)	0 (0.0)	6 (9.7)	0.718	1.308	0.774
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Chalazion	Case	0 (0.0)	2 (8.3)	0 (0.0)	0 (0.0)	2 (3.2)	0.874	2.635	0.695
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Subconjunctival haemorrhage	Case	0 (0.0)	3 (12.5)	7 (26.9)	0 (0.0)	10 (16.1)	0.623	3.378	0.282
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Conjunctival pallor	Case	0 (0.0)	0 (0.0)	14 (53.8)	2 (33.3)	16 (25.8)	27.279	22.454	0.000*
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Pterygium	Case	0 (0.0)	4 (16.7)	2 (8.3)	2 (25.0)	8 (12.9)	0.000	2.379	0.451
	Control	4 (6.5)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.5)			
Allergic conjunctivitis	Case	2 (33.3)	6 (25.0)	6 (23.1)	0 (0.0)	14 (22.6)	0.000	2.098	0.578
	Control	8 (12.9)	0 (0.0)	0 (0.0)	0 (0.0)	8 (12.9)			
Corneal ulcer	Case	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Spontaneous hyphaema	Case	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Iris nodule	Case	0 (0.0)	0 (0.0)	1 |(3.8)	0 (0.0)	1 (1.6)	0.000	2.762	0.999
	Control	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Cataract	Case	0 (0.0)	14 |(58.3)	4 (15.4)	2 (33.3)	20 (32.3)	0.615	13.055	0.003*
	Control	18 (29.0)	0 (0.0)	0 (0.0)	0 (0.0)	18 (29.0)			

***Significant** **OR- Odds ratio**

which patients with genotype AS had increased tendency to develop pterygium (P= 0.028) among leukaemic cases. There was also an increased tendency to haveRoth spots and ARMD among respondents with genotype AS. These findings were statistically significant (p = 0.029 and 0.000 respectively). None of the anterior segment disorders had a significant relationship with the genotype of the children cases and controls. Also none of the other anterior segment disorders hada significant relationship with the genotype ofthe adult cases and controls.

There was a significant difference between the refractive states of the cases and controls (p=0.000). More than two thirds 55 (68.8%) of the cases had hypermetropiacompared to 26 (32.5%) ofthe controls (Table 11).

DISCUSSION

Twenty four (24) eyes (30.0%) among the cases had leukaemic related ocular disorders. This is comparable to low prevalence of ocular disorders of 35.4% reported by Reddy *et al*[8], 39.0% reported by Schachat *et al*[9] in the United State of America and 14.9% reported by Omoti *et al*[2] but markedly different from the high prevalence of 77.8% reported by Eze *et al*[4] and 69.0% reported in Ethiopia by Alemayehu *et al.*[10] The observed disparity may be explained by the fact that this present study included children who are known to have low incidence of leukaemic ophthalmopathy. Also children tend to have the acute fatal disease which claim their lives therefore depriving them of the ophthalmopathy. Reddy *et al*[8] and Schachat *et al*[9] included children in their study hence low prevalence in their study. Eze *et al*[4]and Alemayehu et al[10] who reported high prevalence, studied only adults. Omoti *et al*[11] reported a low prevalence of ocular disorders although their

study was in adults. However some of the studies that reported very high incidence of leukaemic ophthalmopathy may have included disorders which may not necessarily be related to leukaemia. Furthermore this low prevalence may be because only new patients at presentation were included in this study and also the small number of patients were studied. The disparity in incidence of ocular disorder may represent a racial difference but more extensive studies are required to make a definitive conclusion. When the frequency distribution of leukaemic ocular disorders was compared between children and adult cases, 24 out of 80 eyes (30.0%) of all the cases had leukaemic ocular disorders. Ocular disorders were found in 22 out of 66 (35.5%) of the adult eyes against 2 out of 18 (11.1%) of the children eyes. Thus there is an increased frequency of leukaemic ocular disorders among adults compared to children. The 11.1% leukaemic ophthalmopathy in children found in this study is similar to the study by Russo *et al*[12] in which leukaemia eye disorder were detected in 52 of 657 children (9%) suffering from acute leukaemia but different from the study done by Shrestha *et al*[13] in Kathmanda, Nepal in which leukaemic eye disorder were detected in 33 out of 71 children (46.0%) suffering from childhood leukaemia.

TABLE 11: REFRACTIVE STATES OF THE EYES OF CASES COMPARED WITH CONTROLS IN UBTH

Refractive states	Class			Test statistic	p value
	Case n (%)	Control n (%)	Total n (%)		
Hypermetropia	55 (68.8)	26 (32.5)	81 (51.6)	χ^2 = 24.637	0.000*
Myopia	10 (12.5)	10 (12.5)	20 (12.5)		
Emmetropia	15 (18.8)	44 (55.0)	59 (36.9)		
Total	80 (100.0)	80 (100.0)	160 (100.0)		

***Significant**

There was an increased tendency for cases with platelet count less than 150,000/mm to have subconjunctival haemorrhage compared to those with platelet counts greater than 150, 000/mm and this finding was statistically significant (p=0.014). This is line with what is found in literature which explains that thrombocytopenia would lead to increased bleeding tendencies.[14] This further shows the importance of investigating the platelet count of leukaemic patients to monitor their treatment and getting it to a normal value as this may likely reduce the chances of developing subconjunctival haemorrhage, intra-retinal haemorrhage and its attendant complications in patients with leukaemia.

There was no significant association between platelet level and development of anterior and posterior segment disorders in children. The reason for this may be due to the small number of children 9 (22.3%) in this study. There was a statistically significant relationship between subconjunctival haemorrhage (p=0.010), intraretinal haemorrhage (p=0.008) and platelet count in adult cases with platelet counts less than 150, 000/mm.

Proptosis had a statistically significant (p=0.041) relationship with white blood cell count among the anterior segment disorders, with an increased tendency for cases with white blood cell count greater than 20,000 to have proptosis compared to those with WBC count less than 20,000. This was similar to the findings of a case report done in the same hospital by Enosolease *et al.*[15] This implies that the use of WBC count early in the management of leukaemic patients is very important as it may likely reduce the chances of developing proptosis in these patients. This would further prevent the attendant complications of corneal ulceration, opacity and blindness. Thus reducing the prevalence of blindness of leukaemic patients in the country.

There was a significant association for the cases to develop retinal infiltrates, neovascularization, microaneurysms and venous dilation and tortuosity when compared to the controls

(P=0.022, 0.041, 0.041, and 0.022 respectively) among the posterior segment disorders. These findings were in line with literature,[16,17] which explains that the increase in WBC count would lead to increased viscosity in the retinal blood vessels leading to these manifestations.

This study showed a statistically significant relationship for cases with anaemia to develop conjunctival pallor when compared to those with normal PCV. This was also the finding in both children and adults. This finding is similar to finding in other studies[4,15,18] which show an increased tendency to have conjunctival pallor with decrease in PCV. Furthermore, children with anaemia showed a statistically significant tendency to have proptosis, subconjunctival haemorrhage and conjunctival pallor compared to those with normal PCV (p = 0.007). These findings buttresses the importance of PCV as a risk factor for development of ocular complications in leukaemic patients.

There was no significant relationship between genotype and leukaemic ocular disorder. However there was a significant relationship between genotype and pterygium in which patients with genotype AS had increased tendency to develop pterygium, Roth's spots and ARMD (p= 0.028, 0.029, 0.000 respectively) among cases. The reason for this is not certain but may be related to the vascular effects of the sickle cell gene and could serve as the basis for future studies.

Over two thirds 55 (68.8%) of the leukaemia cases had hypermetropiacompared to 26 (32.5%) ofthe controls,while 44 eyes (55.0%) of the control were emmetropic. This was found to be statistically significant (p=0.000). This is similar to the findings by Sharma *et al.*[19]

In conclusion, the risk factors for the development of leukaemic ophthalmopathy include increased white blood cell count, reduced platelet count and low packed cell volume. Higher age was also more likely to have ophthalmic complications.

REFERENCES

1. Ohkoshi K, Tsiaras WG. Prognostic importance of ophthalmic manifestations in childhood leukaemia. Br J Ophthalmol. 1992; 76: 651–655.
2. Shama T, Grewal J, Murray PI. Ophthalmic manifestations of acute leukaemia. The ophthalmologist's role. Eye. 2004; 18:663-672.
3. O'Rourke JF, O'Connor GR. The eye as a sanctuary in acute lymphoblastic leukaemia. Lancet 1980; 1: 452– 456,
4. Eze BI, Ibegbulam GO, Ocheni S. Ophthalmic manifestations of leukaemia in adult Nigerian. Middle East Afr J Ophthalmol 2010; 17: 325-329.
5. Buckley MF, James JW, Brown DE, Whyte GS, Dean MG, Chesterman CN et al. A novel approach to the assessment of variations in the human platelet count. Thromb Haemost 2000; 83:480-484
6. Sing AD. The prevalence of ocular disease in chronic lymphocytic leukaemia, Eye. 2003; 17:3-4
7. WHO Groups of Experts on Nutritional Anaemia. Technical Report Series.WHO, Geneva; 1986.
8. Reddy SC, Jackson N, Menon BS. Ocular involvement in leukaemia- A study of 228 cases. Ophtalmologica. 2003; 217:441-445.
9. Schachat AP, Markowitz JA, Guyer DR, Burke PJ, Karpe JA, Graham ML. Ophthalmic manifestation of leukaemia. Arch Ophthamol. 1989;107:697-700.
10. Alemayehu W, Shamebo M, Bedri A, Mengistu Z. Ocular manifestations of leukaemia in Ethiopians. Ethiop Med J. 1996; 34: 217 – 224.
11. Omoti AE, Omoti CE, Momoh RO. Ocular disorders in adult leukaemia Patients in Nigeria. Middle East Afr J Ophthalmol. 2010; 17:165-168.
12. Russo V, Scott Lu, Querques G, Stella A, Noci N. Orbital and ocular manifestation

of acute childhood leukaemia; clinical and statistical analysis of 180 patients. Eur. J. Ophthalmology. 2008; 18:619-623

13. Shrestha GS, Khadka D, Sharma AK, ShresthaJK.Ocular manifestation of childhood acute leukaemia in tertiary eye centre of Kathmandu Nepal. Nepalese Journal of ophthalmology. 2014;6:197-204
14. Leukaemia. Available at http://en Wikipedia.org/wiki/file: Symptoms of leukaemia. png. (Accessed 9th Jan2014).
15. Enosolease ME, Awodu AO. Proptosis and blindness: An unusual primarypresentation of chronic granulocytic leukaemia.Pak J Med Sci. 2006; 22:326-328.
16. Stephen J, Ryan C, Andrew P, Charles P. Peripheral retinal micro aneurysm inchronicleukaemia. Am J Ophthalmol.1996; 21: 167 – 182.
17. Jampol LM, Goldberg MF, Busse B. Peripheral retinal microaneurysm in chronic leukaemia.Am J Opthalmol.1975;80:242 – 248.
18. Omoti AE, Omoti CE. A review of ocular manifestations of leukaemia.Haema.2006;9:637-41.
19. Sharma T, Grewal J, Gupta S, Muray PI. Ophthalmic manifestations of acute leukaemias: the ophthalmologist role. Eye. 2004;18:663 – 672.