Original Article

Access this article online
Quick Response Code:

Website: www.meajo.org
DOI: 10.4103/meajo.MEAJO_187_16

Predictors of Ocular Surface Squamous Neoplasia and Conjunctival Squamous Cell Carcinoma among Ugandan Patients: A Hospital-based Study

Harrison-Williams C. M. Lloyd, Simon Arunga[1], Amos Twinamasiko[1], Meier A. Frederick[2], John Onyango[1]

Abstract:

AIM: The aim of the study was to assess the predictors of ocular surface squamous neoplasia (OSSN) and conjunctival squamous cell carcinoma (SCC) among Ugandan patients.

MATERIALS AND METHODS: Patients presenting for removal of ocular surface lesions received human immunodeficiency virus (HIV) testing, completed questionnaires about demographic, behavioral, and historical potential risk factors for conjunctival neoplasia, and had lesions examined for interpalpebral versus other locations, rough versus smooth texture, and number of feeder vessels. Biopsies were classified pathologically using standard definitions classified OSSN and SCC. HIV rates were calculated for patients: with OSSN, SCC, and benign lesions. Potential risk factors and gross findings were tested for abilities to predict OSSN and SCC.

RESULTS: One hundred and ninety-five patients presented with 212 lesions in 203 eyes. Nearly 34% of the patients were more than 60 years old, 67% were peasants, 88% spent more than 20 h/week outdoors, and only 10% wore sun protection. No potential risk factors predicted neoplasia. HIV prevalence was 17.1% among patients with OSSN compared to 11.1% among those without OSSN; 42.9% among SCC patients compared to 12.0% among those without SCC. Rough tumor surface (adjusted odds ratio [aOR] = 4.4 and 95% confidence interval [CI]: 2.2–9.1), six or more feeder vessels (aOR = 2.6, 95% CI: 1.3–5.2), and interpalpebral tumor location (aOR = 3.3, 95% CI: 1.5–7.1) predicted OSSN. Only a rough tumor surface (aOR = 34.6, 95% CI: 7.8–153.4) predicted SCC.

CONCLUSION: HIV infection remained a risk factor for OSSN and particularly, SCC, but less so than in the past. Lesions' rough surface, six or more feeder vessels, and interpalpebral location increased OSSN risk. Only a rough tumor surface increased risk for SCC.

Keywords:

Conjunctival squamous cell carcinoma, ocular surface squamous neoplasia, predictors, Sub-Saharan Africa, Uganda

Department of Ophthalmology, Connaught Hospital, Freetown, Sierra Leone, [1]Department of Ophthalmology, Mbarara University of Science and Technology and Ruharo Eye Centre, Mbarara, Uganda, [2]Department of Pathology, Mbarara University of Science and Technology and Global Health Collaboration, Seed Global Health, Boston, Massachusetts, USA

Address for correspondence:
Dr. Simon Arunga, Department of Ophthalmology, Mbarara University of Science and Technology, Kabale Road, Mbarara, Uganda.
E-mail: sarunga@must.ac.ug

Introduction

Squamous cell carcinoma (SCC) of the conjunctiva is the extreme of a spectrum ocular surface squamous neoplasia (OSSN) that ranges from mild to moderate through severe dysplasia (also called carcinoma *in situ*) to invasive SCC.[1,2]

Definitive differentiation between benign and OSSN/SCC lesions requires a histopathologic diagnosis from biopsies.[3] In Sub-Saharan Africa, where histopathology services are limited, demographic, behavioral, clinical-historical risk factors, human immunodeficiency virus (HIV) status, and gross characteristics of lesions are five potential tools for preoperative prediction of

How to cite this article: Lloyd HWC, Arunga S, Twinamasiko A, Frederick MA, Onyango J. Predictors of ocular surface squamous neoplasia and conjunctival squamous cell carcinoma among ugandan patients: A hospital-based study. Middle East Afr J Ophthalmol 2018;25:150-5.

biopsies' histological appearances.[4] This study assesses clinical features that distinguish OSSN from non-OSSN conjunctival lesions. Although there have been several Sub-Saharan reports on the epidemiology of OSSN, to the best of our knowledge, this was the first study in Uganda to describe clinical predictors of OSSN.[5-7]

Materials and Methods

Ethics

The study adhered to the tenets of the Declaration of Helsinki. The Institutional Ethical Review Committee, Faculty Research and Ethics Committee, and Departments of Ophthalmology and Pathology of Mbarara University of Science and Technology (MUST), as well as the Clinical Director of Ruharo Eye Centre all approved the study.

Patients

All patients at Mbarara University and Referral Hospital Eye Centre and Ruharo Eye Centre, who presented for the removal of conjunctival surface masses between September 2014 and March 2015, were asked to participate in this study. Only patients who did not give informed consent or those scheduled for operations not combined with excisional biopsy (e.g., trabeculectomy) were excluded from the study.

Human immunodeficiency virus testing

All patients who agreed to participate were counseled about the study's requirement for an HIV test. When HIV tests were confirmed as positive, patients were offered posttest counseling and then referred to the Immune Suppression Syndrome Clinic at Mbarara Regional Referral Hospital or to similar facilities.

Data collection

Demographic and behavioral factors

Patients responded to demographic questions about: (i) age, divided into five strata of <18, 18–29, 30–49, 50–59, and ≥60 years, (ii) marital status as single, married, or widowed, (iii) occupation as professionals, business people, manual laborers, peasants, or unemployed, and residential setting as rural versus urban. They also reported on six behavioral risk factors: (i) time spent outdoors/week (0–9,10–19, and ≥20 h), (ii) use of eye protection (brimmed hats/caps or tinted ultraviolet light-protecting spectacles), (iii) exposure to chemicals (petrol, kerosene, herbicides, and insecticides), (iv) number of lifetime sexual partners (1, 2–4, and ≥5), (v) alcohol intake (present or absent), and (vi) cigarette smoking (present or absent).

Human immunodeficiency virus status

HIV status was collected as (i) reported as positive or negative, (ii) tested as positive or negative, and (iii) treated with antiretroviral drugs, co-trimoxazole, both, or neither.

Clinical historical factors

Five elements from clinical history were sought: (i) presenting symptoms (foreign body sensation, itching, pain, and poor vision), (ii) presenting signs (tumor and bleeding), (iii) previous eye problems (present/absent), (iv) previous eye surgeries (present/absent), and (v) types of previous eye medical treatment (steroid, antibiotic, traditional eye medicine, and unknown).

Physical examination findings

Twelve results of eye examinations were recorded: (i) visual acuity as > or <6/18 (logMAR 0.4771), (ii) area of conjunctiva affected (interpalpebral vs. noninterpalpebral), (iii) specific locus (site) of mass (limbal, corneo-limbal, bulbar, forniceal, caruncular, tarsal, or canthal), (iv) mass size estimated in mm^2 (<10, 10–19, and ≥20 mm^2), (v) mass shape (flat-topped, undulating [sesamoid], and pedunculated), (vi) extent of mass's pigmentation (pigmented, variegated (mixed), and nonpigmented), (vii) its surface texture (rough or smooth) and presence or absence of (viii) corneal infiltration, (ix) corneal staining, (x) leukoplakia, (xi) number of dilated (feeder) vessels (divided into groups as <6, 6–15, and ≥16), as well as (xii) presence or absence of lymphadenopathy.

Pathologic diagnosis

All the participants underwent conjunctival excisional biopsies which were then processed at MUST Pathology department. Two pathologists independently interpreted the slides using three categories of a standard classification of OSSN (i): mild or moderate dysplasia, (ii) severe dysplasia or conjunctival intraepithelial neoplasia (CIN) (carcinoma *in situ*), and (iii) SCC.[6] In cases of a disagreement between the two pathologists' diagnoses, the pathologists reviewed the cases in question together, to gain a consensus.

Data analysis

The STATA 11.0 statistical program (Stata Corp., LLC 4905, Lakeway Drive College Station, Texas, USA) tested four sorts for association with OSSN:

Demographic characteristics

Demographic characteristics were sex, age, occupation, site of residence, and marital status.

Potential behavioral risk factors

Potential behavioral risk factors were time outdoors, use or not of eye protection, history of toxic chemical exposures, number of sexual partners, and histories of ever alcohol or cigarette exposure.

Human immunodeficiency virus status

Human immunodeficiency virus status was whether HIV positive or negative.

Physical examination findings

Physical examination findings were visual acuity, interpalpebral versus nonpalpebral location, specific tumor site, shape, pigmentation, and surface (ir) regularity, and a number of feeder vessels.

In association tests, first, bi-variance analyses used two-way tables with measures of bivariate association (Chi-square); second, factors with associations at a level of $P < 0.05$ were included in multiple logistic regression models; and third, results of the simplest significant model to established factors firmly associated with OSSN and SCC were reported.

Results

Of 218 biopsies excised from 201 patients during the 7-month study period, 212 biopsies from 195 patients were histologically examined. Eight patients had separate nasal and temporal ocular surface tumors excised from a single eye; seven patients had one ocular surface tumor removed from the right and one from the left eye. One patient had nasal and temporal tumors excised from one eye and a (third) nasal tumor excised from the other eye. The rest of the patients (179) had single biopsies from one eye. Hence, during the 7 months study period, 212 biopsies were harvested from 203 eyes of 195 patients.

Demographic characteristics

The 195 participants had a median age of 48 years, only 18% were <30 years, slightly more than a third (34%) were in the 30–49-year-old age group, and a similar number (also 34%) in the oldest ≥60-year-old age group. The ratio of women:men was 1.2:1. Most patients were married (64%), peasants (66%), and lived in rural settings (76%).

Behavioral characteristics

Nearly 87% of the participants spent more than 20 h/week outdoors, but only 10% used eye protection when outside. Slightly more than a third (34%) reported exposure to at least one of petrol, kerosene, pesticides, or insecticides. Almost 47% of the participants reported a history of alcohol intake, but only 21% reported ever smoking cigarettes. Regarding a number of sexual partners, almost three-quarters of patients (74%) fell into two groups: 42% reported having only one partner and 32% reported having had between two and four partners.

Human immunodeficiency virus status of patients

Of 195 participants in the study, 137 (70%) reported having been tested previously for HIV. Of these, 112 (82%) reported negative previous results. About 180/195 (92%) of patients were tested at the time of study entry. Of these, 152 (84%) had negative results. Almost 25/28 (89%) of test-positive patients reported treatment status: 16 (64%) were on both antiretroviral treatment and co-trimoxazole, 7 (28%) were on co-trimoxazole only, and one patient each received only antiretroviral treatment or no therapy (4% each). There were three new patients who had previously not been aware of their HIV status and were therefore not on any treatment. Prevalence of HIV was higher among those with SCC (42.86%) than among those with OSSN (17.27%).

Presenting complaints

Thirty patients were asymptomatic (i.e., patients scheduled for cataract surgery with a coincidental detection of an ocular surface mass), 15% of patients complained primarily of the conjunctival mass itself, 13% reported eye pain, 9% complained of poor vision, 8% of foreign body sensation, and 5% of itching.

Previous ophthalmologic history

Forty-five percent of patients reported previous eye conditions. Most of these (39% of the entire group) had received medical treatment and 12% had undergone eye surgery. In the medical treatment group, 42% had received treatment of unknown sorts, 34% steroid preparations, 13% traditional eye remedies, and 11% antibiotics.

Ophthalmological examination

Table 1 shows the ophthalmic examination findings of the participants. In the affected eye (excluding 56 patients with cataracts), more than 4 of 5 (81%) patients had a visual acuity better or equal to 6/18 (or logMAR ≥0.4771). Most masses were interpalpebral (79%), their locations either corneolimbal (44%) or limbal (38%), their size ≥10 mm^2, and the number of dilated vessels feeding the mass <6 (68%). The surfaces of most masses were smooth (69%) and their surface shape sesamoid (63%). About half of the masses (52%) were pigmented, slightly <½ (45%) showed corneal infiltration, between a fourth and a fifth (23%) showed leukoplakia, and 15% corneal staining. Lymphadenopathy was associated with conjunctival mass in 76% of patients.

Histological examination results

Three-quarters of all biopsies (147/212: 69.3%) revealed benign lesions (pinguecula and pterygium). Sixty-one of the 65 (93.8%) histologically confirmed neoplastic lesions were either SCC (46/61: 75.4%) or OSSN (15/61: 24.5%).

Features associated with ocular surface squamous neoplasia on initial bivariate analysis

Table 2 shows features which were initially associated with OSSN. Among seven demographic variables (age, sex, marital status, occupation, and occupational location),

Table 1: Distribution of physical examination features among participants (*n*=212)

Clinical feature	Classification	*n* (%)
Presenting visual acuity of affected eyes	<6/18 (or logMAR<0.4771)	27 (19.42)
(*n*=139,we excluded vision of those with cataract)	≥6/18 (or logMAR≥0.4771)	112 (80.58)
Affected area of conjunctiva	Inter-palpebral	167 (78.77)
	Noninterpalpebral	45 (21.23)
Site of tumor	Limbal	81 (38.21)
	Corneal-limbal	93 (43.87)
	Bulbar	24 (11.32)
	Forniceal	3 (1.42)
	Caruncular	1 (0.47)
	Tarsal	9 (4.25)
	Canthal	1 (0.47)
Tumor size (mm^2)	<10	54 (25.47)
	10-19	74 (34.91)
	≥20	84 (39.62)
Tumor shape	Flat-topped	64 (30.19)
	Sesamoid	133 (62.74)
	Pedunculated	15 (7.08)
Degree of pigmentation of tumor	Pigmented	16 (7.55)
	Mixed	85 (40.09)
	Nonpigmented	111 (52.36)
Tumor surface texture	Rough	65 (30.66)
	Smooth	147 (69.34)
Presence of corneal infiltration	Yes	96 (45.28)
Presence of corneal staining	Yes	32 (15.09)
Presence of leukoplakia	Yes	48 (22.64)
Number of dilated (feeder) blood vessels	<6	145 (68.40)
	6-15	62 (29.25)
	≥16	5 (2.36)
Presence of associated lymphadenopathy	Yes	161 (75.94)

LogMAR: Logarithm minimum angle of resolution

Table 2: Physical examination features associated with ocular surface squamous neoplasia on bivariate analysis (*n*=212)

Variable	Variable category	cOR	95% CI	*P*
Tumor surface regularity	Smooth	1.0		<0.001
	Rough	5.1	2.6-10.1	
Presence of leukoplakia	No leukoplakia	1.0		<0.001
	Leukoplakia	9.4	3.8-23.3	
Number of feeder blood vessels	<6	1.0		<0.001
	≥6	3.5	1.9-6.7	
Presence of corneal staining	No corneal staining	1.0		0.0172
	Corneal staining	2.6	1.1-6.0	
Location of tumor	Noninterpalpebral	1.0		<0.001
	Interpalpebral	3.1	1.6-6.3	
Tumor pigmentation	No pigmentation	1.0		0.1197
	Tumor pigmentation present	1.5	0.9-2.6	
Tumor's longest diameter (mm)	<3	1.0	0.6-5.0	0.0676
	3-5.99	1.7		
	≥6	3.0	1.0-9.0	
Tumor shape	Flat-topped	1.0	1.1-3.6	0.0840
	Sesamoid	1.9		
	Pedunculated	1.2	0.4-3.7	
Presence of corneal infiltration	No infiltration	1.0		0.0819
	Infiltration	1.6	0.9-2.8	
Tumor area (mm^2)	<10	1.0	0.8-3.2	0.2134
	10-19.99	1.6		
	≥20	1.9	0.9-3.8	
Tumor site	Limbal	1.0	0.9-3.0	0.2050
	Corneo-limbal	1.6	0.6-4.0	
	Bulbar	1.6		
	Others	0.6	0.2-2.0	
Presence of associated lymphadenopathy	No lymphadenopathy	1.0		0.9855
	Lymphadenopathy present	1.0	0.5-1.9	

OR: Odds ratio, CI: Confidence interval

only older age correlated with OSSN. Among the 9 elements from clinical history, three – (i) presenting complaint of an ocular tumor, (ii) previous disease in the affected eye, and (iii) history of cigarette smoking – were significantly associated with OSSN. Five of 12 tested physical findings initially correlated significantly with OSSN: (i) rough tumor surface, (ii) leukoplakia, (iii) ≥6 feeder vessels, (iv) interpalpebral location, and (v) corneal staining.

Multivariate analysis for associations with ocular surface squamous neoplasia

Only three gross findings – (i) rough tumor surface (adjusted odds ratio [aOR] = 4.4, 95% confidence interval [CI]: 2.2–9.1), (ii) six or more feeder vessels (aOR = 2.6, 95% CI: 1.3–5.2), and (iii) interpalpebral tumor location (aOR = 3.3, 95% CI: 1.5–7.1) – were significantly associated with OSSN on multivariate analysis.

Features associated with squamous cell carcinoma on initial bivariate analysis

Table 3 shows features initially associated with SCC. Among all the demographic, behavioral, and clinical-historical variables tested on bivariate analysis, only (i) increased age and (ii) pain or tumor as presenting complaints correlated significantly with SCC. Among 12 physical examination findings tested, 7 correlated significantly with SCC on bivariate analysis: (i) tumor surface roughness, (ii) leukoplakia, (iii) sesamoid tumor surface shape, (iv) ≥6 feeder vessels, (v) corneal staining, (vi) tumor area ≥20 mm^2, and (vii) corneal infiltration.

Multivariate analysis for associations with squamous cell carcinoma

After adjusting for age, presenting complaint, and all other variables significant on bivariate analysis, only

Table 3: Features from physical examination associated with squamous cell carcinoma on bivariate analysis (*n*=212)

Variable	Classification	cOR	95% CI	*P*
Tumor surface regularity	Smooth	1.0		<0.001
	Rough	34.6	7.8-153.4	
Presence of leukoplakia	No leukoplakia	1.0		<0.001
	Leukoplakia	19.1	6.6-55.3	
Number of feeder blood vessels	<6	1.0		0.0021
	≥6	4.0	1.6-9.8	
Presence of corneal staining	No corneal staining	1.0		0.0025
	Corneal staining	4.6	1.8-11.9	
Location of tumor	Noninterpalpebral	1.0		0.6266
	Interpalpebral	1.3	0.4-4.1	
Tumor pigmentation	No pigmentation	1.0		
	Pigmentation present	2.2	0.9-5.5	0.0726
Tumor's longest diameter (mm)	<3	1.0	0.1-9.3	
	3-5.99	1.1		0.0641
	≥6	3.3	0.4-27.1	
Tumor shape	Flat-topped	1.0		<0.001
	Sesamoid	12.5	1.6-94.9	
Presence of corneal infiltration	No infiltration	1.0		0.0417
	Infiltration	2.5	1.0-6.2	
Tumor area (mm^2)	<10	1.0	0.3-8.4	
	10-19.99	1.5		0.0032
	≥20	6.4	1.4-29.3	
Tumor site	Limbal	1.0	0.8-6.1	
	Corneo-limbal	2.2		0.2743
	Bulbar	1.8	0.4-7.8	
Presence of associated lymph-adenopathy	Absent	1.0		
	Present	0.6	0.2-1.4	0.2191

OR: Odds ratio, CI: Confidence interval

Table 4: Participants characteristics strongly associated with SCC on multivariate analysis (*n*=212)

Variables	cOR	95% CI	aOR	95% CI	*P*
Tumor surface regularity					
Smooth	1.0				0.001
Rough	34.6	7.6-153.4	34.6	7.8-153.4	

OR: Odds ratio, CI: Confidence interval

rough tumor surface emerged as a physical finding significantly associated with SCC on multivariant analysis.

Discussion

Regarding conjunctival OSSN and SCC in Sub-Saharan Africa, we (i) found no significant predictors among demographic, behavioral, and historical risk factors, (ii) quantified amplification of OSSN/SCC by HIV as less than in previous studies, and (iii) demonstrated that rough tumor surface, six or more feeder vessels, and interpalpebral location predict OSSN, while rough tumor surface predicts SCC.

The risk factors for OSSN, older age, tumor as presenting complaint, previous disease in the affected eye, and history of cigarette smoking correlated on bivariate analysis but not on multivariate analysis. For SCC, increased age, positive HIV status, pain, or tumor on presentation correlated on bivariate but not on multivariate analysis. A 2009 Ugandan study also found no significant association on a multivariate analysis between SCC and age, sex, educational level, cigarette smoking, or outdoor occupation.[7] Our study showed no relationship between chronic conjunctival disease and OSSN, contrary to a 1999 Tanzanian series [Table 4].[8]

Multivariate analysis did not show an association between daytime spent outdoors and OSSN/SCC: in contrast, one previous Ugandan study found 7 h outdoors/week associated with OSSN and another found more than 10 h outdoors per week associated with SCC.[2,9,10] Our failure to find such associations is likely due to only 13.8% of our patients spending <20 h/week outdoors: a few unexposed subjects reduce the power of exposed versus unexposed patient comparisons. Being *asymptomatic* failed to exclude ocular surface masses from being OSSN/SCC. Waddell *et al*. also found that 76% of their HIV-positive patients with OSSN were asymptomatic.[9]

HIV prevalence was lower in this study than in previous Ugandan OSSN/SCC series. Twenty years ago, Waddell *et al*. found that 64% of OSSN patients were HIV positive, as opposed to 31% of controls.[11] Among our OSSN patients, 17.3% were HIV positive versus 11.3% positivity in non-OSSN patients. In Ateenyi-Agaba's 2009 study, 85% of SCC patients were HIV positive versus 45% of controls.[7] In our study, SCC patient HIV positivity was 42.9% versus 12% in patients negative for SCC. HIV positivity continued to associate with invasive behavior: HIV positivity in patients with invasive SCC was 42.9%, more than twice the rate of the 17.3% in all OSSN patients. Perhaps, free antiretroviral therapy in Uganda has dampened HIV-amplified progression of conjunctival dysplasia to SCC.[12]

In consideration of conjunctival findings, previous East African studies reported that OSSN masses had more feeder vessels, leukoplakia, gelatinous appearance,[8] and interpalpebral locations than did benign masses.[2,8] In our series, leukoplakia and six or more feeder vessels joined tumor surface irregularity, corneal staining, and sesamoid tumor shape, as associated with OSSN on bivariate analysis, but only rough tumor surface, six or more feeder vessels, and interpalpebral location of tumor remained associated with OSSN on multivariate

analysis. For SCC, on bivariate analysis, rough tumor texture, sesamoid tumor surface, leukoplakia, ≥6 feeder vessels, tumor area ≥20 mm^2, and corneal infiltration correlated, but only rough surface continued to correlate on multivariate analysis.

One key limitation of this study was the inability to measure the CD4 count; this would have helped in revealing any statistical relationship between the degree of immunosuppression and the degree of dysplasia of the ocular surface tumor. This is because of the additional financial implication which was beyond the budget allocation for this study.

Conclusion

Rough tumor surface, six or more feeder vessels, and interpalpebral tumor location increased likelihood of OSSN. Their absence does not exclude OSSN: they cannot, by themselves, triage patients as requiring biopsy. They may contribute to clinical algorithms that differentiate OSSN from non-OSSN; they may also help ophthalmologists appreciate increased likelihood of OSSN, in specific cases. This is especially true for rough tumor surface, the one finding our study linked to SCC.

Acknowledgments

The authors would like to acknowledge Dr. Freddy Mbumba, the Director of Ruharo Eye Centre, for permission to conduct the study, Dr. Daniel Atwiine for helping in analysis, and all the staff of MUST Department of Ophthalmology, MUST Department of Pathology, and Ruharo Eye Centre.

Financial support and sponsorship

The study was supported by Sightsavers Uganda.

Conflicts of interest

There are no conflicts of interest.

References

1. Saornil MA, Becerra E, Méndez MC, Blanco G. Conjunctival tumors. Arch Soc Esp Oftalmol 2009;84:7-22.
2. Newton R, Ziegler J, Ateenyi-Agaba C, Bousarghin L, Casabonne D, Beral V, *et al.* The epidemiology of conjunctival squamous cell carcinoma in Uganda. Br J Cancer 2002;87:301-8.
3. Huerva V, Ascaso FJ. Conjunctival Intraepithelial Neoplasia – Clinical Presentation, Diagnosis and Treatment Possibilities. Intraepithelial Neoplasia: InTech; 2012.
4. Furahini G, Lewallen S. Epidemiology and management of ocular surface squamous neoplasia in Tanzania. Ophthalmic Epidemiol 2010;17:171-6.
5. Gichuhi S, Macharia E, Kabiru J, Zindamoyen AM, Rono H, Ollando E, *et al*. Clinical presentation of ocular surface squamous neoplasia in Kenya. JAMA Ophthalmol 2015;133:1305-13.
6. Gichuhi S, Sagoo MS, Weiss HA, Burton MJ. Epidemiology of ocular surface squamous Neoplasia in Africa. Trop Med Int Health 2013;18:1424-43.
7. Agaba CA. Human Papillomaviruses and their Association with Squamous cell Carcinoma of the Conjunctiva: Institutionen för Medicinsk Epidemiologi och Biostatistik/Department of Medical Epidemiology and Biostatistics; 2009.
8. Poole TR. Conjunctival squamous cell carcinoma in Tanzania. Br J Ophthalmol 1999;83:177-9.
9. Waddell K, Kwehangana J, Johnston WT, Lucas S, Newton R. A case-control study of ocular surface squamous Neoplasia (OSSN) in Uganda. Int J Cancer 2010;127:427-32.
10. Santelli JS, Edelstein ZR, Wei Y, Mathur S, Nalugoda F, Lutalo T, *et al*. 4. Trends in HIV prevalence, incidence and demographic, behavioral, and biological risk factors among youth in Rakai, Uganda, 1999-2011. J Adolescent Health 2013;52:S5.
11. Waddell KM, Lewallen S, Lucas SB, Atenyi-Agaba C, Herrington CS, Liomba G, *et al.* Carcinoma of the conjunctiva and HIV infection in Uganda and Malawi. Br J Ophthalmol 1996;80:503-8.
12. Rubaihayo J, Tumwesigye NM, Konde-Lule J. Trends in prevalence of selected opportunistic infections associated with HIV/AIDS in Uganda. BMC Infect Dis 2015;15:187.