PREVALENCE OF KERATOCONJUNCTIVITIS SICCA IN PATIENTS WITH HIV/AIDS ATTENDING THE COUPLES COUNSELLING CENTRE IN KENYATTA NATIONAL HOSPITAL

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A dissertation submitted in part fulfillment for the degree of masters of Medicine (Ophthalmology), University of Nairobi.

2016

DECLARATION

Principal Investigator

I declare that this research proposal is my original work and has never been published or presented for a degree in any other University.

Dr. Antonella Wanjiku

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DEDICATION

To God, thank You for everything. Start to finish.

To David Muthee. I cannot thank you enough for your unfailing support.

To Miss Muthee. I love you to the moon and back.

TABLE OF CONTENT

LIST OF ABBREVIATIONS

HIV	Human Immunodeficiency Virus
AIDS	Auto Immune Deficiency Syndrome
HIV+	HIV positive
HIV-	HIV negative
DES	Dry Eye Syndrome
KS	Keratoconjunctivitis Sicca
KNH	Kenyatta National Hospital
CCC	Couples Counselling Centre
VA	Visual Acuity
TBUT	Tear Break Up Time
SJS	Steven Johnson's Syndrome

LIST OF FIGURES AND TABLES

ABSTRACT

Background: HIV and AIDS is one of the greatest public health challenges in Sub-Saharan Africa and especially Kenya. HIV/AIDS can affect the eye and cause sight threatening manifestations, including Keratoconjunctivitis sicca. To the best of our knowledge, this is the first study that has assessed keratoconjunctivitis sicca among HIV+ patients in Kenya.

Objectives: To determine the prevalence of keratoconjunctivitis sicca in participants with HIV/AIDS attending the couples counselling centre at Kenyatta National Hospital.

Study design: A cross sectional descriptive study

Study methodology: The study was carried out among HIV+ and HIV- participants who attend the discordant couples counselling centre at Kenyatta National Hospital. After history was taken, we recorded vision and examined participants under the slit lamp. TBUT and Schirmer's test were recorded in a questionnaire.

Results: Out of the 544 participants enrolled, 57 (10.5%) were excluded mainly due to pregnancy. We included 487 participants (54% male, 46% female) of mean age. There were 249 (47% male, 53% female) HIV+ of mean age 39.23 ± 8.53 years (range 22-59 years) and 238 (62.2% male, 37.8% female) HIV- participants of mean age 36.77 $\pm$ 8.25 years (range 21-58 years)

HIV+ participants had a higher prevalence of dry eyes at 30.3% compared to HIV- participants (9.7%) which was statistically significant (p value 0.00, odds ratio 2.8). More HIV+ males had dry eyes (44.4%) compared to the HIV+ females (20.0%). There was no correlation between the CD4 cell count and the severity of the DES among the HIV+ participants (p value 0.98).

Conclusions: The prevalence of DES among HIV+ patients at KNH is comparable to similar studies in temperate regions. There was no correlation between decrease in tear production and the severity of HIV infection. The effect of HAART on DES could not be determined due to small number of participants not on HAART.

INTRODUCTION AND LITERATURE REVIEW

Acquired Immunodeficiency Syndrome (AIDS) is a retroviral disease caused by Human Immunodeficiency Virus (HIV) and is responsible for a progressive failure of the immune system thus resulting in several opportunistic infections and malignancies.

According to the WHO AIDS report of 2014, there were 36.9 million people living with HIV/AIDS with nearly 70% of this population in the sub-Saharan Africa [1]. In Kenya, 1.6 million people were living with the disease by 2012, an overall prevalence of 6.2%. Of these, more than 200,000 couples are discordant, 60-70% of which are female discordant meaning that the female partner is HIV+ while the male is HIV-. Women, who make up 57% of the HIV+ population have a prevalence of 6.9% while men have a lower prevalence of 4.4%. Approximately 315,000 HIV+ patients were on both 1st and 2nd line HAART in Kenya as of December 2009 [2].

Studies have shown that HIV has several ocular manifestations in both the anterior and posterior segments [3]

Dry Eye Syndrome also known as Dry Eye Disease, Keratoconjunctivitis Sicca and keratitis Sicca is defined as multifactorial disease of the tear film and ocular surface that result in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. Common symptoms of DES include dryness, irritation, foreign body sensation, light sensitivity, and itching.

Some of the major risk factors for the development of DES include advanced age, female sex, hormonal imbalance, autoimmune disease, HIV/AIDS, abnormal corneal innervation, vitamin deficiency, environmental stress, contact lens use, infection, medication use, and ophthalmic surgery. A study done in Lublin, Poland by Scot et al confirmed factors listed in the DEWS report of 2007 [4] [5]

It is estimated that almost more than 14-15% Australians 50 years and older have DES, and millions more experience episodic symptoms of dry eye; of these, approximately two-thirds are women. This was according to a study done in the Blue Mountains region of Sydney [6]

Dry eye syndrome can hinder the performance of activities of daily living, and DES is associated with an overall decrease in quality of life. A study done in Salisbury, England showed that persons with DES were more likely to report difficulty in reading [7]

Studies done on HIV+ patients found a prevalence of 17-21% with DES. Lucca et al of the United States did two separate studies on HIV+ males and HIV+ females to arrive at this conclusion [8] [9] and Geier et al in Germany found a prevalence of 23.8% [10]

Other studies done in regions with comparable climate showed higher prevalence of DES in HIV. In India, the prevalence was found to be 53% [11] while in Brazil the prevalence was lower at 25.8% [12]

Several studies have been done in various parts of Africa which have shown that dry eye syndrome affects 10-20 % of HIV+ patients in Morocco [13] and in Ethiopia [14] are a few examples of such studies.

To the best of our knowledge, there are no similar studies here in the country.

DES Etiology and pathophysiology

Dry eyes syndrome comes about as a result of either reduced production of tears as happens in Sjogren's syndrome, high rate of tear evaporation as in patients with cicatricial ectropion and external factors such as low humidity environment and high wind velocity.

The epithelial injury caused by dry eye stimulates corneal nerve endings, leading to symptoms of discomfort, increased blinking and, potentially, compensatory reflex lacrimal tear secretion. Loss of normal mucin at the ocular surface contributes to symptoms by increasing frictional resistance between the lids and globe.

Viruses, including HIV, are postulated to cause DES by triggering an autoimmune reaction targeting the tear producing glands.

A comprehensive flow chart on the same is available in Appendix I.

Dry Eye Severity Grading System

Dry eye syndrome is classified as either mild, moderate or severe depending on patients' symptoms and findings on Schirmer's and TBUT. All studies referenced adhered to the DES grading system of minimum 1 symptom and TBUT less than 10 seconds or Schirmer's less than 10mm per min.

A table summary of this can be found in Appendix II.

Treatment

The principles of treatment of DES are to lubricate the ocular surface, eliminate cause of dryness and prevent further drying.

Tear substitutes are considered to be first-line treatment for mild-to-moderate aqueous tear deficiency. Available formulations include drops, gels and ointments. Behavioral modifications such as increasing blinking rate and avoiding air conditioned spaces also helps improve symptoms. Johnstone, a pharmacist in South Africa wrote and published a comprehensive guideline on the drugs available for treatment of DES [15]

Other treatment options such as surgical intervention are available and will be based on the severity. This is summarized in Appendix III

STATEMENT OF PROBLEM

According to WHO, HIV and AIDS is one of the greatest public health challenges in Sub-Saharan Africa [1]. Kenya is among the African countries with highest HIV prevalence in the world and a larger proportion of the population may be living with HIV/AIDS [2].

HIV/AIDS can affect the eye and cause blinding and life threatening manifestations. Keratoconjunctivitis sicca occurs in most of HIV infected individuals at some point during the course of their illness, which can lead to visual impairment and blindness if untreated. Studies have shown that there is some association between HIV/AIDS and DES and have given different prevalence of DES [9] [10] [11] With that there is no generalizable figure for the prevalence of DES among HIV+ patients. In addition, there is limited literature on DES among the couples attending KNH. Therefore, there is need to assess keratoconjunctivitis sicca among HIV+ patients in Kenya.

RATIONALE

With the advent of HAART and comprehensive care, patients living with HIV and AIDS are expected to have a much higher life expectancy, and therefore more cases of HIV related eye conditions including dry eyes will be encountered.

Dry eye syndrome is frequently overlooked despite its impact on the quality of life. This is the first study at KNH to quantify the number of persons living with HIV/AIDS who are affected by DES, and compare findings with similar studies globally.

Our results will enlighten Primary care physicians on the impact of DES on their patients, and guide policy formulation on comprehensive care of patients living with HIV/AIDS to identify, treat or refer cases of DES.

OBJECTIVES OF THE STUDY

Main Objective

To determine prevalence of keratoconjunctivitis sicca among patients living with HIV/AIDS attending the couples counselling center at Kenyatta National Hospital.

Specific Objectives

1. To determine prevalence of DES among patients with HIV/AIDS at Couples Counselling Centre, Kenyatta National Hospital in Kenya and compare it to that of HIV- participants.
2. To determine the relationship between CD4 cell count and presence/severity of DES
3. To determine the relationship between use of HAART and DES in participants with HIV/AIDS at Kenyatta National Hospital

METHODOLOGY

Study Design

A cross sectional descriptive study was conducted in patients with HIV/AIDS and their HIV-partners attending the couples counselling center at Kenyatta National Hospital

Study Period

The study was conducted between April 2014 to April 2015.

Study Area

The study was carried out in Kenya at the couples counselling center (CCC) of Kenyatta National Hospital (KNH), a teaching and referral hospital in Nairobi city. The CCC at KNH caters strictly to discordant couples: only one partner is HIV+ while the other remains negative. The clinic serves an average of 20 patients per day.

Study Population

The study population comprised of HIV/AIDS patients and their partners attending the couples counselling center at Kenyatta National Hospital.

Inclusion Criteria

- Consenting adults (Patients aged of 18 years and above),
- HIV+ with up to date CD4 cell count (not done more than 6 months from date of 1st contact with investigator) and their partners
- HIV- patients with documented results 3 months or less from time of study.

Exclusion Criteria

- No recent CD4 cell count {>6 months}
- Confounding factors and comorbidities {Diabetes, corneal scars, contact wearers, SJS, arthritis, patients already on treatment for DES, oral contraceptive pills, pregnancy}
- Patients under 18 years

Sample Size

The Fisher formula was used to estimate the sample size for the audit files as shown below.

The Fisher formula was used to estimate the sample size for the patients to be studied as shown below.

$$n = \frac{Z^2 \times p \times q}{d^2}$$

$$n = \frac{1.96^2 \times 0.17 \times 0.83}{0.05^2} = 217$$

Where;

n = sample size

p = estimated prevalence of DES amongst HIV+ patient (estimated to be 17% [11])

Z = confidence level at 95% (corresponding to a standard Z value of 1.96)

q = 1- p

d = margin of error (0.05)

Therefore, n =172 patients

Allowing a 10% margin for errors, we arrive at a figure of 189 patients.

Procedure

Patients were recruited at the CCC clinic during their regular visits. We filled a questionnaire for all couples attending the KNH CCC who consented to participate in the study to confirm eligibility. Filtering was done at two levels: The first level of filtering was performed from the questionnaire at the CCC; all those with confounding factors such as diabetes, pregnancy and others listed above were exempted from the study while the rest proceeded for examination by the researcher which entailed the following. VA using Snellen chart. If patient found to have a

refractive error, he/she was referred to the eye clinic for refraction. Slit lamp examination was done to assess eye lashes and conjunctiva for crusts, tear margin meniscus, frothy discharge and conjunctival injection. Demographic details of patients were recorded including gender, age and nationality. Detailed history of ocular complaint and CD4 cell count was recorded.

The second level of filtering was after examination whereby we exempted any patient found to have confounding ocular diseases such as Steven Johnson's disease, corneal scars and others.

The eligible participants underwent Schirmer's test using sterile commercial strips as follows:

a. The eye was gently dried of excess tears using a clean tissue
b. Topical Tetracaine eye drops were applied; the filter paper folded 5mm from one end and inserted at the junction of the middle and outer third of the lower lid, taking care not to touch the cornea or lashes.
c. The participant was asked to keep the eyes gently closed
d. After 5 minutes, timed with a stopwatch, the filter paper was removed and the amount of wetting from the fold measured and recorded.
e. Less than 10 mm of wetting is considered abnormal and was considered a positive test.

TBUT was estimated in the following manner:

a. A moistened impregnated fluorescein strip was instilled into the lower fornix.
b. Participant was asked to blink several times, and then stare straight ahead.
c. Tear film was examined at the slit lamp with a broad beam using cobalt blue filter. After an interval, black spots or lines appear in the fluorescein stained film indicating the formation of dry areas.
d. TBUT is the interval between the last blink and the appearance of the first randomly distributed dry spot. The TBUT was recorded in seconds.
e. A TBUT of less than 10 seconds is abnormal and was considered a positive test.

The sequence was repeated three times for each eye, with the exception of the first step (a.) as long as there is adequate amount of fluorescein still in the eye. An average of the three readings was taken as the TBUT of the participant.

A diagnosis of DES was made if the participant reported presence of at least one of the symptoms often and had either one or both of the diagnostic tests being positive. Those found to have DES were given a prescription with appropriate medication to buy and referral note given for follow up depending on the severity.

Other incidental findings of other ocular manifestations of HIV/AIDS were also catered to; the participant received a prescription or a referral note to the eye clinic depending on the findings and the severity.

Materials

Instruments used include:

- Questionnaire {Appendix 1}
- Snellen's Chart
- Slit lamp
- Fluorescein strips
- Schirmer's Test strips
- Tetracaine Eye drops
- Stop watch
- Laptop

Data Management and Analysis

Data collection

Primary data collection was done on a pre-designed questionnaire (*appendix V*), that was administered via the open source electronic survey tool Limesurvey. This tool was chosen for ease of data collection and subsequent analysis. The tool is web-based and allows responses to be entered directly into a database via an online form. The tool also allows for printable versions of the questionnaire to be produced and filled in offline should the need arise. The investigator read out the questions to the participants and filled out the answers in the questionnaire. The primary means of filling the form was the electronic version with the printed, paper version available as a fallback option. The questions related to symptoms are based on the six item questionnaire

validated by a large population based study in the United States [7] The clinical and diagnostic findings were filled out for each participant.

Where necessary the questions were translated verbally into Swahili for ease of communication. Also for any gaps in information, the participant files were used to supplement and confirm information given by the participant.

Variables

Dependent variable

- Presence/ severity of DES

Independent variables

- Age
- Sex
- Other co-morbidities
- CD4 counts
- Duration on HAART
- Visual Acuity

Data Management and Editing

Since data was directly entered into the online database it was managed and manipulated via the Limesurvey interface. Any printed (paper) questionnaires was scanned into Limesurvey via queXF and verified for correctness. The tool queXF takes scanned paper forms and reads them. The Limesurvey printed questionnaire is queXF compatible.

Data Storage

Data was stored on the online database, a compressed backup of which was stored on the laptop of collection as well as on a separately stored flash disc (external hard disk/drive).

All data was stored under lock and key and with password protected files under the custody of the principal investigator to prevent any illicit access to the data. Use of coded data was done to ensure maximum confidentiality. At the end of the study, the raw data was destroyed and deleted from any existing hard copies by paper shredding and formatting and deleting from any soft copy storage devices including computers, flash discs and hard disks.

Data Analysis

Data analysis was done using the STATA, Version 12 (Stata Corp, College Station, Texas). The collected data was extracted and exported to STATA for Analysis.

Descriptive analysis was done to determine means, frequencies and proportions of the various variables and findings presented by means of tables and charts where appropriate. Chi-square test and logistic regression analysis was used to assess for any relationships between presence of DES and other variables such as gender, CD4 counts and HAART. Confidence level will be taken as 95% ($p < 0.05$) where applicable.

ETHICAL CONSIDERATION

Ethical approval was sought from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee and given.

Informed consent was obtained from all those participating in the study. Assurance was given that the information collected will be used for educational purposes only and any information volunteered will be held in confidence.

All procedures carried out on the participants were non-invasive and caused minimal discomfort to the participants. Also it was ensured that all stains and filter papers to be used were sterile before introduction into the eyes of the participants.

All participants found to have DES were commenced on treatment. A referral to the appropriate clinic was made for participants with other incidental ocular findings during the study.

Confidentiality was maintained throughout the study.

RESULTS

Response Rate

Out of the 544 enrolled participants who consented to be studied, 487 (89.5%) were included (Figure 1) and 57 (10.5%) were excluded (Table 1).

Figure 1: Flow chart of participants enrolled onto the study

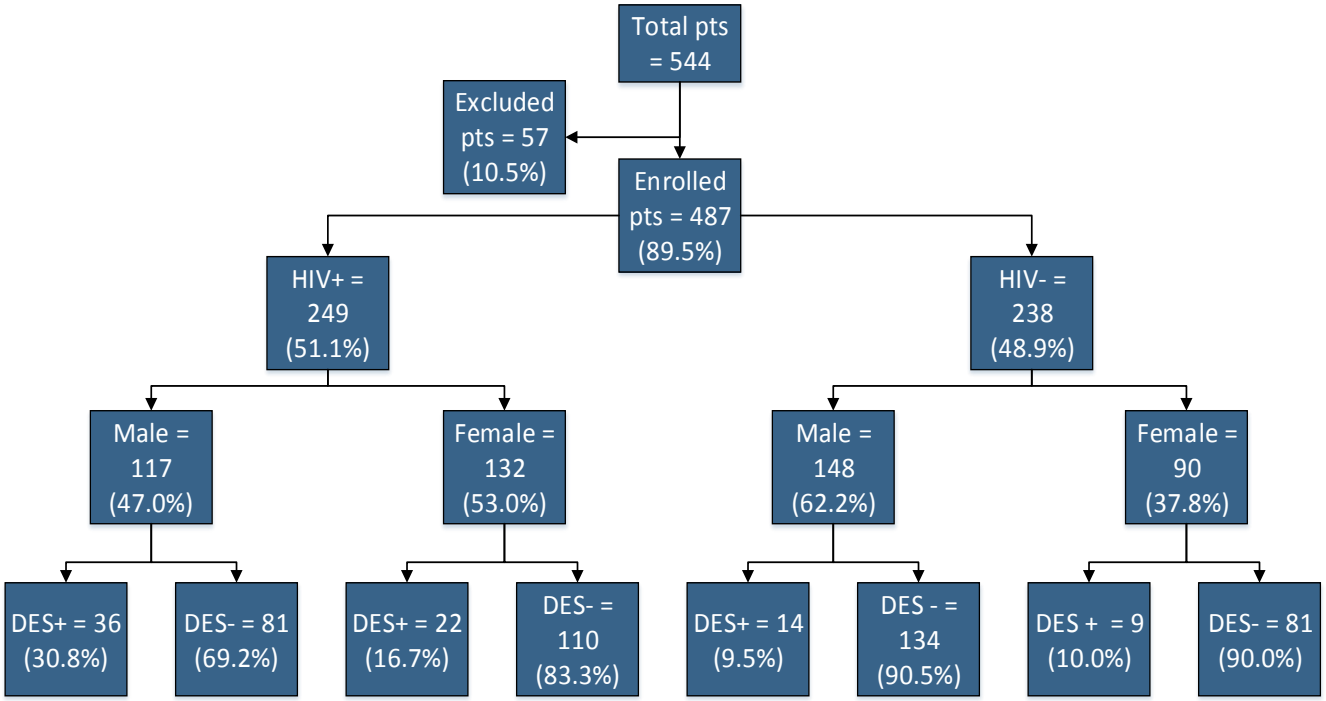
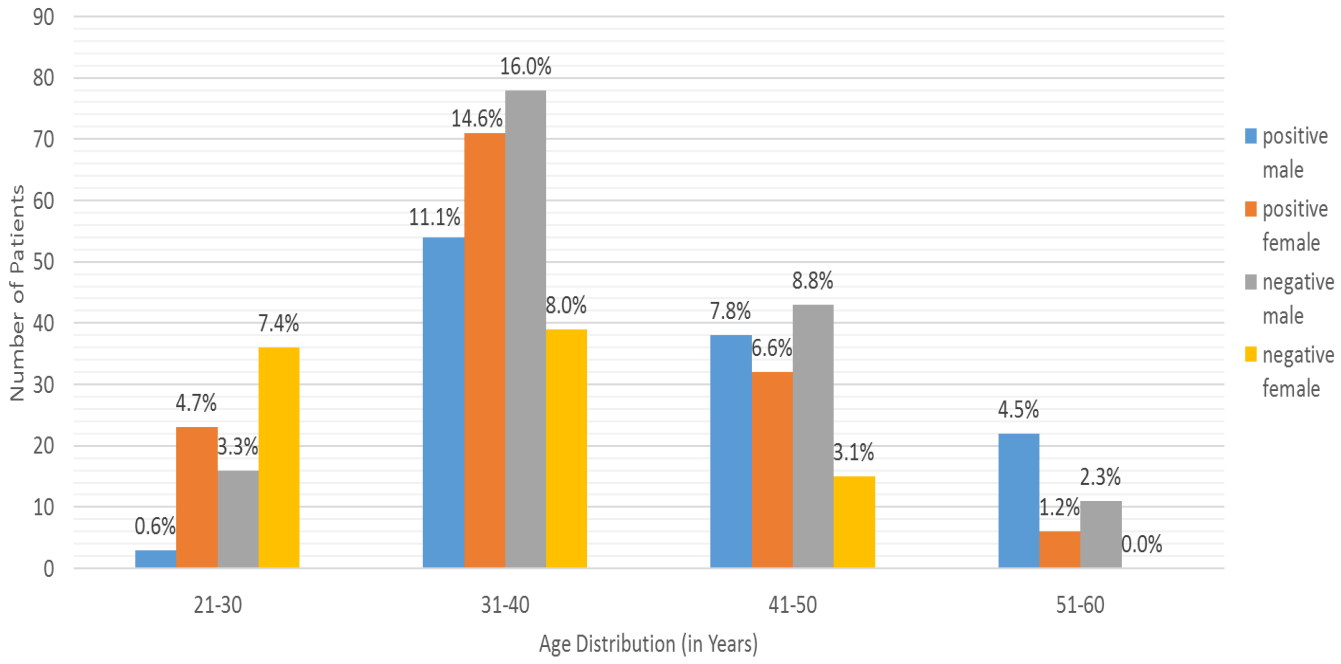


Table 1: Excluded participants and reasons for exclusion

Reason for exclusion	No. of Pts excluded (n=57)	Comments
Pregnancy	27 (47%)	Concurrent study on pregnant women at the DCC
Use of ocular drops	7 (12%)	Only 4 out of the 7 could remember the drug name as Probeta N
Conjunctivitis	7 (12%)	Both infectious and allergic
Trauma	6 (11%)	
Use of Oral contraceptive pills	5 (9%)	
Diabetics	3 (5%)	
Arthritic participants on treatment	2 (4%)	2 females over 55yrs of age

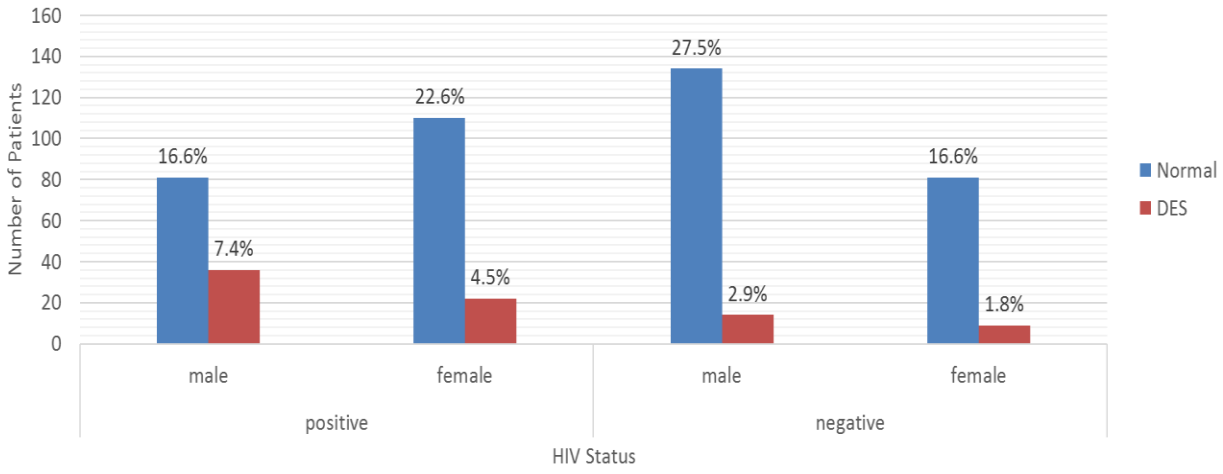
Figure 2: Distribution of participants by age, sex and HIV status (n=487)



Most participants, both HIV+ and HIV –ve, were in the age group of 31-40 years, and were of similar age range.

- HIV+ : 22-59 yrs (mean 39.23 ± 8.531 yrs)
- HIV- : 21-58 yrs (mean 36.77 ± 8.248 yrs)

Figure 3: Distribution of Participants by HIV status and presence of DES (n=487)



The prevalence of DES in:

- All the HIV+, both males and females = 30.3%**.**
- All HIV- = 9.7%. (Odds ratio 2.8, p value 0.00).
- HIV+ males = 44.4%, HIV- = 9.7%.
- HIV+ females = 20.0%: HIV- = 11.1%.

Table 2: Relationship between HIV Status and Presence and severity of DES

DES	Total (n=487)	HIV Status		P Values
		Positive	Negative	
Combined (n=487)				
Normal	406	191 (47.0)	215 (53.0)	0.00
Presence of DES	81	58 (71.6)	23 (28.4)	
Total	***487***	***249***	***238***	
DES severity(n=81)				
Mild	39	26 (66.7%)	13 (33.3)	0.34
Moderate	24	18 (75.0)	6 (25.0)	0.66
Severe	18	14 (77.8)	4 (22.2)	5.19
Totals	81	58	23	

The prevalence of DES in HIV+ was statistically significant (p = 0.00). However, the severity of the DES was not affected by the HIV status.

Table 3: Relationship between CD4 Cell Count and severity of DES

DES	Total (n=249)	CD4 Count			P Values
		<200	200-500	>500	
Combined (n=249)					
Normal	191	34 (17.8)	83 (43.5)	74 (38.7)	0.914
DES Present	58	10 (17.2)	27 (46.6)	21 (36.2)	
total	249	44	110	95	
DES severity (n=58)					
Mild	26	4 (15.4)	13 (50.0)	9 (34.6)	0.884
Moderate	18	4 (22.2)	10 (55.6)	4 (22.2)	0.326
Severe	14	2 (14.3)	4 (28.6)	8 (57.1)	0.165
Total	58	10	27	21	

There was no statistically significant association between CD4 cell count and presence or severity of DES among HIV+ participants (p = 0.91)

Table 4: Relationship between HAART and presence of DES

Total HIV+(n=249)		Use of HAART		P Values
		Yes	No	
No DES	191	182 (95.3%)	9 (4.7%)	0.01
DES present(n=58)				
Mild	26	22 (84.6%)	4 (15.4%)	0.98
Moderate	18	14 (77.8%)	4 (22.2%)	0.34
Severe	14	13 (92.9%)	1 (7.1%)	0.32
Total	**58**	**49**	**9**	

There was a statistically significant difference in presence of DES in HIV+ participants using HAART compared to those not using HAART (P = 0.01). The severity of DES did not appear to be affected by use of HAART. However, due to the low numbers of participants not on HAART, this finding is not conclusive.

Table 5: Relationship between Social History and presence of DES

Social History	Total (n=489)	DES		P Values
		No DES	Presence of DES	
Smoke Cigarette				
Yes	65	32 (49.2%)	33 (50.8%)	0.00
No	422	374 (88.6%)	48 (11.4%)	
Take Alcohol				
Yes	22	16 (72.7%)	6 (27.3%)	0.17
No	465	390 (83.9%)	75 (16.1%)	
Take Coffee				
Yes	34	24 (70.6%)	5 (15.7%)	0.04
No	453	382 (84.3%)	133 (29.4%)	

Cigarette smokers had a higher prevalence which was statistically significant (P = 0.00).

Coffee drinkers had a lower DES prevalence than non coffee drinkers which was statistically significant (P = 0.04)

DISCUSSION

Demographic data

There was neither a statistical significant difference between males and females (M: F = 1.19:1, p-value=0.05) nor between the HIV+ and HIV- participants (HIV+: HIV- = 1.01:1, p-value=0.43), which eliminated bias (figure 1).

Most of our participants (mean age 37.93 years) were in the 31 – 40 years old age group corresponding to the peak age of HIV in the general population in Kenya [2]. HIV+ participants (mean age 39.23, range 22-59 years) had comparable age with HIV- participants (mean age 36.77 years, range 21-58 years) (Figure 2). This is similar to other DES studies to exclude confounding age-related DES in those above 40years [9]

Very few (7%) HIV+ participants were not on HAART because they were newly recruited undergoing initial counselling before they could commence HAART (Appendix IV). The standard procedure in care of a discordant couple is to start the reactive partner on HAART regardless of CD4 cell count, hence almost all were on HAART. To the best of our knowledge, here is no comparable study on discordant couples.

Prevalence

The prevalence in the HIV+ group in our study (30.3%) was comparable to other parts of the world (Appendix V); in USA Lucca et al (17% female, 21% male) [8] [9], in Germany Geier et al (23.6%) [10], in India Gowda et al (53%) [11] , in Brazil Rodriguez (25.8 %) [12] .The main reason for higher prevalence in Kenya, Brazil and India than Germany and USA is likely to be the tropical climate which contributes to the DES.

Compared to other studies in Africa, the difference in our prevalence was most likely due to different study methodologies. In Morocco, Lamzaf et al found a prevalence of 10-20% [13] and in Ethiopia, Bekele et al found a lower (11.3%) prevalence and correlation between DES and CD4cell count [14] However Bekele et al neither used the standard questionnaire nor considered the patients' symptoms as per DEWS guidelines [4]

In normal population studies females have more prevalence of DES than males mainly due to the estrogen effect after menopause [5] [6]. However, in our study (figure 3), males had a higher prevalence of DES than females (Males 44.4%, females 20.0%) similar to USA [9], India [11] and Brazil [12] (Appendix V). We have not found a clear explanation for this contradictory finding and may require further investigations out scope of our current study.

In our study, the HIV- combined prevalence of 9.7% was similar between females (11.1%) and males (10.5%) (figure 3). In Nigeria, Onwubiko et al found higher prevalence (19.2%) [16] perhaps due to the significantly younger age group in our study

Other factors associated with DES:

In our study, we evaluated our participants on the effect of cigarette smoking, coffee drinking, and alcohol use (Table 5)

Participants who smoked cigarettes(were more likely to have DES ($p = 0.00$). which is similar to reports by Moss et al that found a two-fold increase in the risk of DES in participants who smoked; the effect of cigarette smoke on DES is believed to be due to the direct irritant effect to the eyes [17]

Participants who took coffee frequently had a statistically significant reduction in risk of DES ($p = 0.04$) which was similar to USA [17]. It is known that topically applied xanthine can stimulate tear production, thereby decreasing tear film osmolarity and relieving dry eye symptoms. Therefore, as a xanthine, Caffeine may explain this protective effect on DES.

There was no statistically significant increase in risk of DES in participants who consumed alcohol regardless of the frequency.

CONCLUSION

The prevalence of DES is higher in HIV+ participants (30.3%) compared to HIV- pts (9.7%).

The CD4 cell count did not correlate with the presence or severity of DES.

Use of HAART was associated with lower prevalence of DES but the subjects not on HAART were too few to compare.

LIMITATIONS

The greatest limitation was the absence of tear osmolarity tests which has 100% positive predictive value and would have made the results even more reliable.

Most of our study participants were on HAART. This is a practice that is done regardless of CD4 count in order to protect the HIV- partner. Due to this, there were very few HIV+ participants not on HAART making it difficult to analyse the effect of HAART on DES

It is possible that HIV- participants were HIV+ due to the window period effect meaning that they could have acquired the virus since their last date of testing. The documented conversion rate (HIV- partner becoming positive) at the CCC was less than 1%

Although the criteria used to determine DES was relatively stringent, the overlap in symptomatology between DES and allergic conjunctivitis is a limitation that may have influenced the outcome.

RECOMMENDATIONS

Patient symptoms should be given greater consideration in making the diagnosis of DES.

Educate HIV+ patient and HCW on effect of DES and treatment

Scheduled routine (annual) eye check of HIV+ patients in eye clinics

A randomized control trial may further our understanding of effect of use of various drugs used in HIV such as anti TB medication, HAART on DES.

Future study to determine association between DES and viral load

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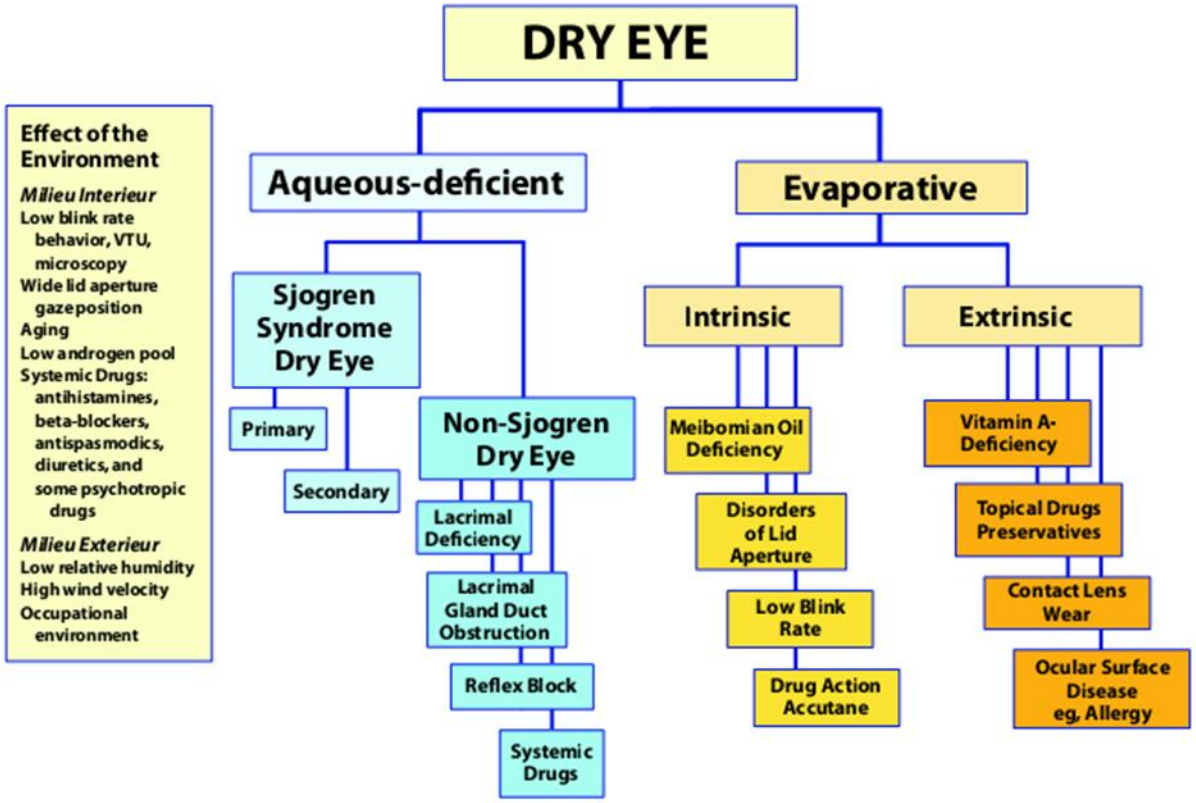
APPENDICES

Appendix I: Etiology of Des



Appendix II: Summary Grading of Dry Eyes

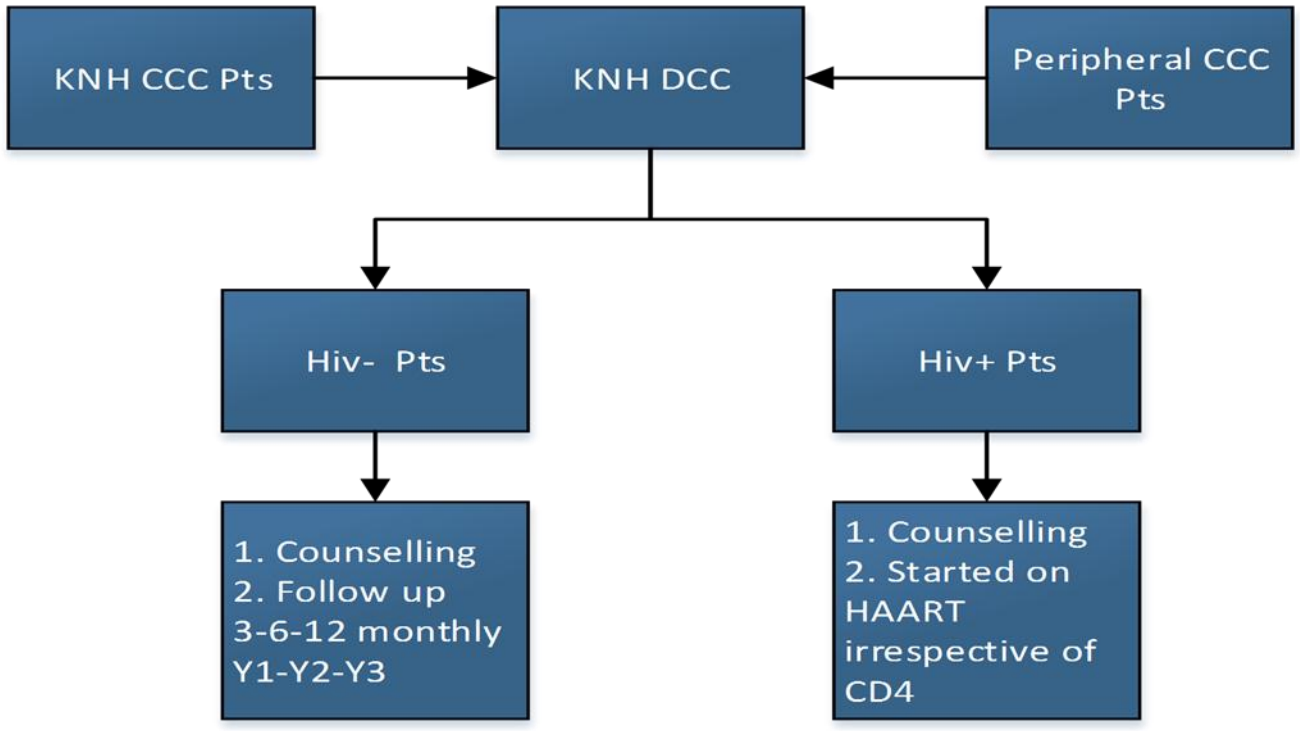
Dry-Eye Severity Level	1	2	3	4*
Discomfort, severity & frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic, stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity-limiting episodic	Annoying, chronic and/or constant, limiting activity	Constant and/or possibly disabling
Conjunctival injection	None to mild	None to mild	+/–	+/++
Conjunctival staining	None to mild	Variable	Moderate to marked	Marked
Corneal staining (severity/location)	None to mild	Variable	Marked central	Severe punctate erosions
Corneal/tear signs	None to mild	Mild debris, ↓ meniscus	Filamentary keratitis, mucus clumping, ↑ tear debris	Filamentary keratitis, mucus clumping, ↑ tear debris, ulceration
Lid/meibomian glands	MGD variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
TBUT (sec)	Variable	≤10	≤5	Immediate
Schirmer score (mm/5 min)	Variable	≤10	≤5	≤2

*Must have signs AND symptoms.

Appendix III: Summary of Des Treatment Guidelines and Options

Severity	Therapeutic Options
Mild	Artificial tears with preservatives up to 4× daily Lubricating ointment at bedtime Hot compresses and eyelid massage
Moderate	Artificial tears without preservatives 4× daily to hourly Lubricating ointment at bedtime Topical anti-inflammatory treatment (cyclosporine A 0.05% 2× daily) Reversible occlusion, lower puncta (plugs)
Severe	All of the above Punctal occlusion (lower and upper) Topical serum drops (20%) 4–6× daily Topical corticosteroids (nonpreserved if available) Moist environment (humidifier, moisture shields) Tarsorrhaphy (lateral and medial) Bandage lenses (rarely)

Appendix IV: Flow of Patients into the DCC



Appendix V: Table showing Comparison of studies

Country	Sample Size (M+F)	DES in HIV (M+F)	DES in HIV+ Males	DES in HIV+ Females	Authors
Kenya-KNH	**249 (117 + 132)**	**30.3%**	**44.5%**	**20%**	**Our study**
India	50	**53% (M = 64%, F = 36%)**			Gowda et al[9]
Brazil	120 (74 + 46)	25.8%			Rodriguez et al[10]
USA	101 (42 + 59)		21%	17%	Lucca et al[15]
Germany	72	23.6%			Geier et al[16]

Appendix VI: Informed Consent

TITLE: PREVALENCE OF KERATOCONJUNCTIVITIS SICCA IN PATIENTS WITH HIV/AIDS ATTENDING THE COUPLES COUNSELLING CENTRE IN KENYATTA NATIONAL HOSPITAL

Patient study identification number----------Date ----------

My name is Dr. Wanjiku Muthee, a postgraduate student at the department of Ophthalmology, University of Nairobi.

I am conducting a study on Dry eye syndrome in HIV+ patients who attend clinic at Couples Counselling Centre at Kenyatta National Hospital. The study is for academic purposes and any information you provide will be treated with confidentiality and your name and other personal information will not appear anywhere in the final write up. Your decision to enroll onto the study or refrain from doing so will in no way affect your treatment at the hospital.

Should I find any eye problem such as need for spectacles etc., I will either write you a prescription for the appropriate medication or write you a referral to the appropriate consultant for further management.

Approval for this Study has been given by the Kenyatta National Hospital/University of Nairobi ethics committee {KNH/UON-ERC}.

I will be available to answer any questions that will help you understand the nature of the study. If you wish to seek any clarification, kindly contact me on **0721777012.**

Procedure

A questionnaire will be provided. It should take approximately 10-15 minutes to complete. We researchers will be available to guide you through the question. If you agree to participate in the study, you will be requested to fill in a questionnaire with the assistance of the researcher. This study will involve answering questions some of which are personal others medical and then will be followed by a thorough examination of your eyes. Your partner will also go through a similar

process in order to compare the difference in findings between HIV+ and HIV- patients. The examination will include putting drops in your eyes, putting strips in the eyes and shining light into your eyes. This will be slightly uncomfortable but I will be using local anesthetic drops on the eyes to make this as comfortable as possible. There will be no residual effects of the drops or the examination. The questionnaires in which this information will be filled will have no personal identifiers to protect your confidentiality.

Risks/Discomfort

There is no risk associated in participating in this study. There will be no invasive procedures that will be carried out in this study that may cause harm to you. Refusal to participate will not change any treatment that you or your child will receive while at the clinic.

Benefits

There will be no direct benefit in participating in the study, Participation in the study is voluntary, but in case you have any questions the interviewer will readily assist you. If you choose not to participate, you will not be denied any service. You will be free to withdraw from the study at any time and at the same you will get your health services provided completely.

Confidentiality

Strict confidentiality will be maintained at all times. There shall be no mention of names or identifiers in the report or publications which may arise from the study. Each participant in the study will be identified by use of codes in order to link them with their results and the data collected will only be accessible to the investigators.

Persons to contact

If you have any questions regarding the study, you may contact Dr. Wanjiku Muthee on mobile number **0721777012**.

If you have any question on your rights as a research participant you can contact the Kenyatta National hospital ethics & research committee by calling 2726300 Ext 44355.

Your participation in the study will be highly appreciated.

CONSENT FORM

I ----------having received information on the study, benefits, risks hereby AGREE/DISAGREE (cross out as appropriate) to participate in the study. I understand that participation is voluntary and I am free to withdraw at any time.

Participant's signature----------date----------

I ----------declare that I have adequately explained information to the participant/ parent (guardian) on the study, benefits and risks and given her time to ask questions and seek clarification regarding the study. I have answered all the questions to the best of my ability.

Investigator's signature----------date----------

FOMU YA IDHINI

TITLE: PREVALENCE OF KERATOCONJUNCTIVITIS SICCA IN PATIENTS WITH HIV/AIDS ATTENDING THE COUPLES COUNSELLING CENTRE IN KENYATTA NATIONAL HOSPITAL

Nambari ya mgonjwa----------Tarehe ----------

Jina langu ni Daktari Wanjiku Muthee, mwanafunzi katika Idara ya Masomo ya Macho katika Chuo Kikuu cha Nairobi.

Ninafanya utafiti kuhusu ugonjwa wa kukauka au ukavu wa macho kwa wagonjwa wanaougua ukimwi pamoja na wake au waume zao ambao huhudumiwa katika kliniki hapa Couples Counselling Centre katika hospitali kuu ya Kenyatta. Utafiti huu ni kwa mujibu wa kuongeza ujuzi wetu kuhusu ugonjwa huu. Ninakuhakikishia kwamba mambo ambayo utaniambia kukuhusu kwa mfano jina lako nitayaweka siri na hautatambulika binafsi kama mojawapo ya watu waliofanyiwa utafiti huu. Matibabu yako hapa hospitalini hayata badilika ama kuadhiriwa kwa vyovyote ukichagua kujiunga na utafiti huu au la.

Iwapo nitapata shida yoyote kwenye macho yako kama kuhitaji miwani, nitakuandikia dawa za kununua au nikutume kwa wataalamu wa shida hiyo ili waweze kukusaidia.

Idhini ya kufanya utafiti umepewa na Kenyatta National Hospital/University of Nairobi ethics committee {KNH/UON-ERC}.

Nitakuwa wakati wote ili niweze kujibu maswalii yoyote amabyo yatakuwezesha kuelewa utafiti huu zaidi. Kwa swali lolote wasiliana nami kwa nambari ya simu: **0721777012.**

Utaratibu

Tutapeana karatasi ya kujibu maswali. Itachukuwa kama dakika 10-15 kujaza maswali. Wanaofanya utafiti watakuwa ili wakusaidie kujaza karatasi ya kujibu maswali. Ukikubali kujumuika na utafiti huu, utahitajika kujibu maswali ya utafiti na utasaidiwa na wanaofanya utafiti. Utafiti huu utakuwa na maswali kuhusu wewe binafsi na mengine kuhusu ugonjwa wa ukimwi iwapo unaugua. Macho yako yataangaliwa kwenye mashine halafu uwekewe dawa

kwenye macho na stripu za karatasi zakupima pamoja na kutumia mwangaza ili kuangalia macho yako vizuri. Mke au mume wako pia atafanyiwa vivyo hivyo ili tuweze kulinganisha kati ya walio na wasiokuwa na ugonjwa wa ukimwi. Kupimwa kutakukera kidogo lakini nitatumia dawa ya kufa ganzi ili kupunguza kukera huko. Dawa na mbinu nitakazotumia hazina madhara kwa macho yako. Majibu ya utafiti yatabaki kuwa siri.

Madhara.

Utafiti huu hauna madhara yeyote. Hautadungwa dawa yeyote au kutolewa kitu chochote kwa mwili kwa sababu ya utafiti. Iwapo utakataa kushiriki, hili halitabadilisha matibabu yako wakati unapokaa kwa hospitali.

Manufaa.

Matokea ya utafiti yatakuwa ya manufaa kwa washikadau na wafanyikazi katika Kitengo cha afya haswa kwa kuimarisha matibabu ya wagonjwa wengine. Kujihusisha na utafitii huu ni kwa hiari na mswali yoyte yatajibiwa na yule anaye kuuliza maswali. Iwapo utaamuwa kutojihusisha na utafitii huu basi hutakatazwa kuendelea na kupokea matibabu katika kliniki. Unaweza kujiondoa katika utafitii huu wakati wowote na bado utaendelea kupokea huduma katika hospitali hii.

Ya siri.

Wewe kama mhusika, utajulikana kwa nambari tu na sio kwa jina lako. Majibu ya utafiti yatabaki kuwa siri na hayataruhusiwa kuonekana na mtu mwingine bila ruhusa yako. Matokeo ya utafiti kwa jumla yatapewa washikadau ambao wanahusika na mipango na matibabu ya macho ya wagonjwa wa ukimwi.

Kama una swali lolote, wasiliana na mtafiti mkuu; Daktari Wanjiku Muthee, nambari ya simu **0721777012**.

Kama una swali kuhusu haki yako kama mshiriki, unaweza kuwasiliana na Kamiti ya haki na utafiti katika hospitali kuu ya Kenyatta nambari ya simu 2726300 Ugani 44355.

FORMU YA KURUHUSU KUFANYIWA UTAFITI

Mimi ----------nimeelewa maana na jinsi utafiti huu utakavyofanyika, na nimepeana idhini baada ya kuelezwa kuhusu madhara na manufaa yake. NIMEKUBALI/NIMEKATAA (futa moja ya haya mawili) kushiriki katika utafiti huu na ninafahamu kuwa ni wa kujitolea na nina uhuru wa kujiondoa.

Sahihi ----------Tarehe ----------

Mimi ----------natangaza kuwa nimepeana habari ya utafiti huu kwa mhusika huyu haswa kuhusu madhara na manufaa na nimekubali kuulizwa maswali na nimeyajibu kwa uwezo wangu wote.

Sahihi ya mtafiti----------Tarehe----------

Appendix VII: Questionnaire

TITLE: PREVALENCE OF KERATOCONJUNCTIVITIS SICCA IN PATIENTS WITH HIV/AIDS ATTENDING THE COUPLES COUNSELLING CENTRE IN KENYATTA NATIONAL HOSPITAL

INSTRUCTIONS

For yes (Y) or No (N) questions, please tick (√) or cross out (—) the response that applies to you

Form Serial Number: _____

KNH CC Patient File Number: _____

1. *Bio data:*

   i. Patient Clinic Code:
   ii. Age in Years:_
   iii. Sex (Tick one): (a)M (b)F

HIV/AIDS History

   iv. On HAART: Y/N
   v. CD4 count: Lowest _____
   Current _____

2. *Past Ocular History:*

Question	No	Yes: Right eye details	Yes: Left eye details
1. Have you ever suffered trauma to the eye?			
2. Have you ever had eye surgery			
3. Are you on follow up or have been followed up for any eye problems			
4. Have you used eye drops?			
5. Have you ever used Contact Lenses?			

3. *Past Medical History:*

   Do you suffer or have suffered from any of the following…..

   i. Diabetes? Y/N
   ii. Thyroid disease: Y/N
   iii. Arthritis? Y/N
   iv. Hypercholesterolemia? Y/N

4. *Obstetric History: -women*
    i. Are you expectant? Y/N or N/A
    ii. Are you on Oral Contraceptive Pills?

5. *Social History:*
    i. Do you smoke cigarettes? Y/N
    ii. Do you take alcohol? Y/N
    iii. Do you take coffee? Y/N

6. *Ocular complaints:*
    How often do you get the following sensations or see these signs in your eyes? (Tick the applicable response)

RE LE

Symptoms	Never	Rarely	Often	Sometimes	All the time
Sandy/Gritty feeling					
Eye pain/burning					
Itching					
Crusts on the eye lashes					
Sticking together of lashes in the morning					

7. *Examination Findings*

VA

RE	LE

Slit Lamp Exam

	RE	LE
Crusts		
Redness		
Discharge		
Height of tear meniscus		

Schirmer's Test (millimeters)

RE	LE

TBUT (seconds)

TBUT	RE	LE
1st reading		
2nd reading		
3rd reading		

Conclusion

DES	RE	LE
None		
Mild		
Moderate		
Severe		

ACKNOWLEDGEMENT

My sincere gratitude goes to:

Maryanne Wanjugu. How is it you knew I would be an ophthalmologist before I started medicine? You are an amazing woman. Thank you for your support and prayers.

My girls Victoria Kimonye, Karimi Munyi, Rebecca Nandasabba, Wandia Kinywa, Mary Ngome, Kate Murianki, Carol Muthumbi, Christine Muthumbi, Beatrice Murage and Victoria Simiyu for listening to me complain and panic and for encouraging me to keep at it. Love you!!

My REAL group members, both old and new, and members of my MEG. Thank you for praying though you did not understand what this was or what the big deal was.

My supervisors. You have been real mentors. Thank you.

My statistician Alex. Your dedication and speed was astounding.

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