OCULAR MANIFESTATIONS IN RHEUMATOID ARTHRITIS PATIENTS ATTENDING THE RHEUMATOLOGY CLINIC AT THE KENYATTA NATIONAL HOSPITAL

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A THESIS PROJECT PRESENTED IN PARTIAL FULFILLMENT FOR DEGREE OF MASTER OF MEDICINE (OPHTHALMOLOGY), FACULTY OF MEDICINE, DEPARTMENT OF OPHTHALMOLOGY, UNIVERSITY OF NAIROBI

DECLARATION

I declare that this research project was my original work and had never been published or presented for a degree in any other University.

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TABLE OF CONTENT

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS AND ACRONYMS

ACPA	–	Anti-Cyclic Citrullinated Peptide Antibody
ACR	–	American College of Rheumatology
BCVA	–	Best Corrected Visual Acuity
CIRD	–	Chronic Inflammatory Rheumatic Diseases
DMARDs	–	Disease Modifying Antirheumatic Drugs
EULAR	–	European League against Rheumatism
JRA	–	Juvenile Rheumatoid Arthritis
PUK	–	Peripheral Ulcerative Keratitis
RA	–	Rheumatoid Arthritis
RF	–	Rheumatoid Factors
TBUT	–	Tear Break-Up Time

ABSTRACT

Background: RA is the most common systemic autoimmune disease and affects middle aged women three times more often than men in a percentage of 0.5 - 2% of the general population. Approximately 25% of patients with RA will have ocular manifestations. Dry eye is the most common ophthalmic manifestation, with a reported prevalence of 15-25%. In our setting there was no recent study on ocular manifestations in patients with RA and this study was to address this gap.

Objective: To determine the prevalence and pattern of ocular manifestations in patients with rheumatoid arthritis at the rheumatology clinic of Kenyatta National Hospital.

Methods: This was a cross-sectional study done in Kenyatta National Hospital rheumatology clinic between April 2017 to May 2018. The study population included patients who are 18 years above diagnosed with Rheumatoid arthritis according to the 2010 ACR/EULAR criteria for the diagnosis of RA by rheumatologists at KNH. The patients were consecutively enrolled in the study during their clinic visits. Statistical analysis was done using the SPSS program version 23.0. Ocular manifestations were presented as percentages and chi square test used to test associations.

Results: Fifty-nine (59) patients were studied. The mean age was 51.4 years and 89.8% were females. More than a third had more than 5 years' duration of the RA disease. Ocular manifestation was diagnosed in 96.6% of the patients and some patients had more than one manifestation. Dry eye syndrome was the most common manifestation at 93.2% while others had cataract (22%) and episcleritis (10.2%). DES and cataracts were associated with older age and those on steroids had a lower prevalence of blepharitis (p=0.040). Duration of RA disease was not associated with ocular manifestations. Visual acuity was normal for 93.2% of the patients.

Conclusion: The prevalence of ocular manifestations is very high in RA patients mainly due to DES which occurs in 9 out of 10 patients

Recommendation: All patients diagnosed with RA should be referred to an ophthalmologist for evaluation of ocular co-morbidities.

CHAPTER ONE: INTRODUCTION

1.1 Introduction

Rheumatoid arthritis (RA) is one of the most common systemic autoimmune inflammatory diseases [1]. Primarily the target structure of the disease is the synovial joints but extra-articular structures may be involved [2]. RA is an autoimmune systemic disease characterized by a symmetrical, destructive, deforming, inflammatory polyarthropathy in association with a spectrum of extraarticular manifestations and circulating antiglobulin antibodies, termed rheumatoid factors (RF) [3] [4].

RA affects middle aged women three times more often than the men in a percentage of 0.5 - 2% of the general population [5]. Despite exhaustive research, the precise cause of RA remains unknown. Although a variety of cells play a role in RA disease, macrophages may be of particular significance in the disease process [6]. For instance, Tumor Necrosis Factors alpha (TNF-α) is found to be overproduced in joints of patients with RA and can induce an increase in synoviocyte proliferation and a cascade of secondary mediators involved in the recruitment of inflammatory cells [5] [6].

Extra-articular manifestation in RA are more common in seropositive patients [7]. Approximately 25 percent of patients with RA will have ocular manifestations [8]. These may include keratoconjunctivitis sicca, scleritis, episcleritis, keratitis, peripheral corneal ulceration, and less common entities such as choroiditis, retinal vasculitis, episcleral nodules, retinal detachments, and macular edema [8]. Dry eye is the most common ophthalmic manifestation of RA, with a reported prevalence of 15-25% [8]. Dry eyes due to RA are classified as secondary Sjogren's syndrome [9].

1.2 Justification

There are very few studies that have attempted to determine the ocular manifestation in patients with RA. In addition, a better understanding of the different types of ocular involvement associated with RA permits the timely management of potentially serious sight-threatening complications. This study attempts to address this issue and would be used to create awareness for ophthalmologists to counsel their patients

1.3 Objectives

To determine the prevalence and pattern of ocular manifestation in patients with rheumatoid arthritis attending the rheumatology clinic at Kenyatta National Hospital.

The specific objectives of this study will be:

1. To determine the prevalence of ocular manifestation in patients with RA.
2. To identify different types of ocular involvement in patients with RA.

CHAPTER TWO: LITERATURE REVIEW

2.1 Ocular manifestations in patients with rheumatoid arthritis

2.1.1 Keratoconjunctivitis Sicca

Keratoconjunctivitis sicca, or dry eye syndrome, is the most common ocular manifestation of RA and has a reported prevalence of 15 to 25 percent [1]. Keratoconjunctivitis sicca, or dry eye syndrome, is commonly seen in patients suffering from systemic autoimmune disease, and RA is the most common autoimmune disorder associated with dry eye [10].

RA patients with dry eye commonly develop dry eye secondary to lymphocytic and plasma cell infiltrate of the lacrimal gland that lead to destruction of acini in the lacrimal glands. Characteristic complaints include itching, burning, foreign body sensation, and photophobia. The severity of the symptoms correlates with the age and duration of RA but does not correlate with the severity of arthritis [10] [11].

Use of artificial tear substitutes and punctal plugs are usually necessary to counter the symptoms of severe dry eye in patients with RA. Topical Cyclosporine a (CsA) is approved by the FDA for the treatment of dry eye. Cyclosporine A is a fungal-derived peptide that inhibits T-cell activation and consequently inhibits the inflammatory cytokine production seen on the ocular surface of patients with dry eye and RA [12] [10].

2.1.2 Episcleritis

Episcleritis is the inflammation of superficial layers of the sclera. Episcleritis presents as a relatively asymptomatic acute onset injection in one or both eyes. Other symptoms may include eye pain, photophobia, and watery discharge. Its prevalence among patients with

RA has been reported to be 0.17–3.7%. Rheumatoid episcleritis affects women more frequently than men and is most common in the sixth decade of life [13].

Most cases of episcleritis are self-limiting, but patients may find some relief with topical lubricants, non-steroidal anti-inflammatory agents, or corticosteroids. If unresponsive to topical therapy, systemic non-steroidal anti-inflammatory agents may be useful [13].

2.1.3 Scleritis

Anterior scleritis is a painful and potentially blinding inflammatory disease that presents with a characteristic violet-bluish hue with scleral edema and dilatation. With posterior scleritis, patients may present with a white eye, but with severe retrobulbar pain. Fundus exam may also reveal chorioretinal granulomas, retinal vasculitis, serous retinal detachment and optic nerve edema with or without cotton-wool spots [14].

Although scleritis may be the initial sign of rheumatoid disease, it usually presents more than ten years after the onset of arthritis. Multiple studies have found that patients with scleritis have more advanced joint disease and more extra-articular manifestations than do rheumatoid patients without scleritis [13] [15]. Although subcutaneous nodules appear in 20–30% of patient with RA, their presence increases to approximately 50% in patients with scleritis [13]. Pulmonary disorders, such as pleural effusion, lung nodules, pneumonia are more common in rheumatoid patients with scleritis than in patients who do not have scleritis. In addition, cardiac manifestations, including pericarditis, valvular disease, conduction abnormalities, and myocardial ischemia are more common in RA patients who have a history of scleritis [15]. Exacerbation of scleritis often occurs at times of increased RA activity.

Scleromalacia perforans is a rare form of necrotizing anterior scleritis. It presents with progressive thinning of the sclera without significant redness or pain. The blue-black hue of the sclera is a result of the melanocyte-laden choroidal layer of the eye becoming visible through the thin sclera [16].

The mortality rate is higher in patients with RA with scleritis when compared to patients with RA without scleritis [16] 36–45% of patients with scleritis and RA will be dead within three years of the onset of scleritis if left untreated with systemic medications. This compares to a three years' mortality rate of 18% in RA patients without scleritis. Death is usually secondary to extra-articular vasculitis. Necrotizing scleritis is associated with a higher mortality than the other forms [14].

Treatment of scleritis almost always requires systemic therapy, as topical therapy is generally insufficient. The use of nonsteroidal anti-inflammatory drugs, corticosteroids, or immunomodulatory drugs is usually necessary in the treatment of scleritis [14].

2.1.4 Peripheral Ulcerative Keratitis (PUK)

Peripheral ulcerative keratitis (PUK) refers to a crescent shaped destructive inflammation of the juxtalimbal corneal stroma associated with an epithelial defect, presence of stromal inflammatory cells, and stromal degradation. It is a destructive process mediated by collagenolytic and proteolytic enzymes released from neutrophils and/or macrophages that result in peripheral corneal stromal degradation [1].

Patients with PUK frequently present with pain, tearing and photophobia. Although topical management may lead to some symptomatic relief, the main treatment of PUK is the treatment of the underlying systemic vasculitis [14].

2.1.5 Retinal Vasculitis

RA can be associated with retinal vascular inflammation, which is a serious and potentially blinding condition. Retinal vasculitis is generally painless and patients may be asymptomatic or present with a variety of symptoms, including decreased visual acuity, visual floaters, scotomas, decreased ability to distinguish colors, and metamorphopsia [17] [9].

Active vascular disease is characterized by exudates around retinal vessels resulting in white sheathing or cuffing of the affected vessels. However, many patients may show no clinical signs on exam, and fundus fluorescein angiography may be necessary to detect areas of retinal swelling, exudation, and macular edema. Severe retinal vasculitis requires adequate inflammation control using corticosteroids or immunomodulatory therapy [17] [11].

2.2 Past Studies on Ocular Manifestations in Patients with Rheumatoid Arthritis

2.2.1 Global

Globally a number of studies have been conducted on ocular manifestations in patients with RA. In India, Charanya *et al* [18] carried out a study to determine the prevalence of ocular manifestations in patients with RA and to find out the ocular complications of the routine drug therapy followed to treat RA. A study in Iraq by Al-Bedri *et al.* [3] evaluated the ocular manifestations in patients with RA. Lamba et al. [17] outlined several common

ocular complications associated with RA. Kumar [19] in Nepal identified different types of ocular involvement in cases of Adult RA and Juvenile RA in a tertiary care hospital in Nepal and compared the prevalence of those ocular findings among them. In a study by Zlatanović *et al.* [20] presented different ocular manifestations of RA and their frequency. Yet another study by Ammapati *et al.* (2015) determined the ocular manifestations of rheumatoid arthritis and correlated the role of anti-cyclic citrullinated peptide antibody (anti-CCP antibody) with the ocular manifestations [21].

Literature reveals that a cross-sectional study is the most common study design employed on ocular manifestations in patients with RA studies. Charanya *et al* [18] conducted a one-year prospective clinical study of 50 RA patients. Ocular examination included best corrected visual acuity, color vision, detailed slit lamp and fundus examination, refraction, intraocular pressure measurement, and tests for dry eyes. Al-Bedri *et al.* study [3] was a cross sectional study conducted on 103 patients with RA diagnosed according to either the 1987 revised ACR criteria or the 2010 ACR /EULAR criteria for diagnosis of RA. Baseline demographic and clinical characteristics of patients were recorded. Ocular manifestations were assessed in all patients. Kumar study [19] was hospital based cross-sectional study, patients below 15 years of age were included in the Juvenile Arthritis group. Detailed systemic and ocular history was taken as per the proforma and detailed ocular examination was carried out. Paired t-test was used as the statistical tool to find out the significant difference. Zlatanović *et al* [20] examined 691 patients with the diagnoses of RA. All examined patients were in I or II stage of the disease according to the criteria of ACR. Ammapati *et al.* (2015) was also a cross-sectional study that examined 299 eyes of the 196 rheumatoid arthritis patients [21].

On results, Charanya *et al* [18] found out that about 85% were female patients and 15% male patients. Steroid toxicity in the form of posterior sub capsular cataract was seen in 5 patients. Ocular manifestations of RA were seen in 32 patients out of which the most common was dry eyes followed by scleritis, episcleritis, iridocyclitis, and secondary glaucoma. Al-Bedri *et al.* [3] found the mean age of the RA patients was 41.5 years with a female to male ratio of 7.6: 1. Dry eyes were the most frequently identifiable ocular manifestation (27.2%) followed by drug induced ocular disease (12.6%). Bhadoria *et al.* [22] established that patients with RA, 19.63% were observed to have ocular changes. Of these keratoconjunctivitis sicca in 19 (17.7%) patients and episcleritis in one (0.93%) were attributable to RA. In Kumar's [19] study among 50 cases of arthritis 33 cases showed ocular involvement (25 from RA group and seven from JRA group). Among them, the most common ocular manifestation was dry eye 22% followed by uveitis in nine percent. Zlatanović *et al* [20] found that the most common manifestation of ocular involvement was keratoconjunctivitis sicca. Episcleritis was diagnosed in 5.06% patients with RA, while scleritis was present in 2.06% of patients. Ammapati *et al.* (2015) found out that 77 patients (135 eyes, 39%) out of the 196 patients studied had ocular manifestations typical of rheumatoid arthritis. Dry eye was the most common manifestation (28%, 54 patients). Of the patients, 78% were females (60 patients) [21].

Charanya *et al* [18] concluded that a regular ophthalmologic evaluation should be done in all RA patients even though they are asymptomatic to ensure early identification of ocular involvement and thus to help alleviate the problems of visual impairment and blindness. Other previous studies also recommend the need for timely diagnosis and treatment of rheumatoid arthritis in order to prevent vision threatening consequences [19] [17]. Studies

also concluded that ocular manifestations are a significant part of the extra-articular manifestation of rheumatoid arthritis [21].

2.2.2 African Region

Studies on ocular manifestations in patients with rheumatoid arthritis are few in Africa. The few studies that have been conducted do not specifically focus on general ocular manifestations but narrowed to specific ones. For instance, Noche *et al.* in 2016 [23] determined the profile of ophthalmic manifestations in CIRD. Yet another study in the same year by Noche *et al.* [24] examined rheumatoid polyarthritis suspected in an HIV infected patient with scleritis, peripheral ulcerative keratitis, and anterior uveitis.

Noche *et al.* [23] conducted an observational study with cases of CIRD presenting RA (n = 16), systemic lupus erythematosus (n = 8), ankylosing spondylitis (n = 8), mixed connective tissue disease (n = 2), scleroderma (n = 1), and juvenile idiopathic arthritis (n = 1). Ophthalmic manifestations were found in 22 (61.1%) patients who presented with dry eye syndrome (n = 7), cataract (n = 6), anterior uveitis (n = 6), glaucoma (n = 4), and suspected maculopathy (n = 1). They also reported a case of a 37-year-old female, diagnosed with AIDS and who was on antiretroviral therapy for the past 2 years. Ophthalmic workup was negative for opportunistic infections and potential causes of scleritis and peripheral ulcerative keratitis. Based on ACR/ EULAR and considering the good response to the treatment (sulfasalazine), diagnosis of RA was made in the absence of confirmatory lab tests.

Noche *et al.* concluded that in the context of ocular manifestations associated with polyarthropathies, coexisting pathologies should be considered. Diagnostic workup of

chronic inflammatory rheumatism should be carried out, even in the context of HIV infection [23] [24].

A rare study conducted in Kenya by Mathenge in 1995 carried out a prospective cross-sectional study at KNH to study ocular manifestation of RA. During a period of 12 months 86 patients with confirmed RA were included in the study. The main ocular complication of RA seen was keratoconjunctivitis sicca (11.6%) and episcleritis (1.2%). Keratoconjunctivitis sicca was more frequent with increasing duration of RA. Mathenge concluded that the visual disability arising from ocular complications of RA was not serious except where keratoconjunctivitis sicca occurred concurrently with cataracts [25].

CHAPTER THREE: MATERIAL AND METHODS

3.1 Study Design

This was a cross-sectional hospital-based study.

3.2 Study period

April 2017 to July 2018

3.3 Study Area

The study was done at the Rheumatology Clinic in Kenyatta National Hospital (KNH) located in Nairobi, Kenya. Nairobi is the capital and largest city of Kenya with a population of 3.36 million in 2011 [26]. Kenyatta National Hospital is one of the biggest teaching and referral hospital in East African region and the largest in Kenya, located in the capital city Nairobi. The hospital is about 3-4 kilometers from the city has Capacity of 2,519 beds. It serves as primary hospital serving residents of Nairobi and referral patients from different places across Kenya. KNH also serves as the main teaching hospital for College of Health Sciences University of Nairobi for both undergraduates and post-graduates. The rheumatology clinic is one of the specialized clinics in the medical department, it serves all clients referred from different parts of the country who needs further management and follow up. The clinic offers services to patients once a week with an average number of patients ranging between 25 to 40. This number includes all patients with all types of connective tissue disorders with an average of 5-10 patients with Rheumatoid Arthritis.

3.4 Study Population

This included patients with RA who are diagnosed by rheumatologist and fulfill the 2010 ACR/EULAR criteria for diagnosis of RA [1].

3.5 Sample Size

The following sample size determination formula for finite population correction was used to estimate the proportion of population study size [27].

$$n^1 = \frac{NZ^2\mathrm{P}(1-P)}{d^2(N-1) + Z^2\mathrm{P}(1-P)}$$

Where

n' = sample size with finite population correction,

N = size of the target population = 120 (estimated minimal number of RA patients seen in the Rheumatology Clinic in KNH is approximately 10 patients per week according to the registry book in one month)

Z = statistic for 95% level of confidence = 1.96

P = estimated proportion of ocular manifestation of patients with RA – 12.8%

d = margin of error = 6.4%

$$n^1 = \frac{120 * 1.96^2 * 0.128(1-0.128)}{0.064^2 * (120-1) + 1.96^2 * 0.128(1-0.128)}$$

$$n^1 = 56$$

3.6 Sampling procedure

Patients who attended rheumatology clinic in KNH for management of rheumatoid arthritis were approached, the study explained to them and consent to participate was sought. Those who consented to participate were consecutively enrolled into the study until the desired sample size was achieved. This audit was done in all patients who met the inclusion criteria during the period of January 2018 to March 2018.

3.7 Inclusion Criteria

Adult patients aged 18 years and older were included in this study

3.8 Exclusion Criteria

Patients with other medical conditions that are associated with ocular complications such as diabetes, hypertension, and thyroid disease were excluded.

3.9 Outcome Measures

Ocular examination included:

1) Best corrected visual acuity
2) Intraocular pressure

3.10 Case Definition

Case definition is a patient diagnosed to have rheumatoid arthritis by a rheumatologist.

3.11 Examination methods

For the purpose of this study, the conditions listed below was diagnosed as follows: [28]

1. **Dry eye syndrome:**

   a) Tear Break Up Time (TBUT) of less than 10 seconds is considered abnormal. Severe dry eyes less than 4 seconds, moderate dry eyes between 4-7 seconds and mild dry eye between 8-9 seconds

   b) Schirmers test 2 (less than 10 millimeters of wetting after 5 minutes)

2. **Uveitis:** (see grading tables below)

   a) Anterior - presence of cells and or flare in the anterior chamber and one or more of the followings: ciliary injection, Keratic precipitates, hypopyon and miosis.

b) Intermediate – presence of cells, haze or condensation in the anterior vitreous phase and or evidence of anterior uveitis.

c) Posterior – presence of choiroiditis and or retinitis.

d) Panuveitis – evidence of inflammation of all the layers of the uvea.

3. **Scleritis:** Inflammation of anterior or posterior layer of the sclera.
4. **Episcleritis:** Inflammation of superficial layer of the sclera.
5. **Peripheral ulcerative scleritis:** progressive melting and ulceration of the peripheral cornea.
6. **Retinal vasculitis:** Inflammation of retinal vessels.

Table 1:Grading of cells in anterior chamber [28]

Cells per field	Grade
0	No cells
1-2	Rare cells
3-7	Occasional cells
7-10	1+cells
10-20	2+ cells
20-50	3+ cells
>50	4+ cells

Table 2:Grading of flare in anterior chamber [28]

Flare	Grade
0	No flare
Faint flare (barely detectable)	1+
Moderately (iris and lens detail clear)	2+
Marked flare (iris and lens detail hazy)	3+
Intense flare (fixed coagulated aqueous humour with considerable fibrin)	4+

Table 3:Grading of Vitreous Opacity [28]

Vitreous Haze	Grade
No opacities	0
Few opacities but fundus clearly seen	1+
Scattered fine and coarse opacities with somewhat obscured fundus	2+
Many opacities with marked blurring of fundus	3+
Dense opacities prevent a view of the fundus	4+

3.12 Data Collection Procedure

Consent to participate was also sought from patients diagnosed with RA. Data was collected by semi-structured questionnaire. The questionnaire was pre-tested at KNH and participants in the pre-test was not included in the study. Prior to the recruitment the principal investigator went through the patients' files to identify those diagnosed with RA after which eligible patients are recruited. The principal investigator was assisted by one research assistant whose role was; to help to identify possible candidates, translation and preparation of participants for eye examination.

Assistants were trained for one day on details of research procedure. After recruitment, the participant underwent eye examination as per the questionnaire. Detailed systemic and ocular history was taken as per the questionnaire and likewise detailed ocular examination was carried out. Visual Acuity was evaluated using Snellen chart for literate and E chart for illiterate patients. Examination of lid and adnexa was performed with help of torchlight. Conjunctiva, episclera, sclera and anterior segment was examined using slit lamp. In cases of suspected episcleritis and scleritis diffuse natural light was used for evaluation.

For the evaluation of cells in the anterior chamber, the widest slit lamp beam at 1.00 mm height with maximum luminance of Haag-Streit slit lamp was used. Grading of cells and flare in the anterior chamber was done according to Hogan's classification. Vitreous opacities were evaluated with slit lamp and graded with direct ophthalmoscope according to Hogan's classification. Fundus was examined after the full dilatation of pupil; the fundus examination was carried out with +90 D lens. Intraocular pressure was taken by Goldman applanation tonometer using slit lamp biomicroscope.

Tear Break Up Time (TBUT) was done by instilling a local anesthetic drop into the patient's eye, applying fluorescein in the lower fornix, patient instructed not to blink and a slit lamp with a cobalt blue beam. It was recorded as the number of seconds that elapsed between the last blink and the appearance of the first dry spot on the tear film. Less than 10 second considered dry eye

Schirmer's test was carried out using sterile commercial strip, using a clean gauze the eye was gently dried of excess tears. The rounded end of the test strip was inserted at the junction of the middle and outer third of the lower lid of each eye, taking care not to touch lashes or cornea, patient was asked to close to keep the eyes gently closed. After 5 minutes timed with a stopwatch, the test strip was removed and the amount of wetting reed from the calibration and recorded. less than 10 millimeters of wetting are considered dry eye. Photos were taken for unique cases of RA for further consultation. Consultations with other medical specialties were sought in cases wherever it was felt necessary.

3.13 Data Management and Analysis

All the filled questionnaires were checked by the principal investigator for completeness. Collected data was coded and entered into a Microsoft excel spreadsheet. Statistical analysis was done using Statistical program for social sciences (SPSS) program version 23. Categorical variables were analyzed using frequencies and percentage. Continuous variables were summarized using mean, percentile, range, and standard deviation, where appropriate. Prevalence of ocular manifestations was presented as a percentage. Similarly, the types of ocular manifestations were presented as proportions. Independent t test was used to compare means between two groups and chi square test to test associations between

two categorical variables. For each outcome variable, based on the univariate analysis, any associations with a p-value of <0.05 was included in a multivariable analysis according to strength of association.

3.14 Ethical Considerations

Ethical approval was sought from KNH/UON Ethics and Research Committee. Permission to conduct the study was also sought from the administrative head of KNH. Patient details and identity was kept anonymous at all times through the use of coded questionnaires with matching codes on the patient's file. The information on the questionnaire was only accessible to the primary investigator and statistician who upheld confidentiality and adhered to data protection standards.

Data was stored only in a computer with a password to facilitate confidentiality. This study aimed to produce results which contributed towards evidence-based practice in the management of ocular manifestation in RA patient. As such, hopefully the results will be published and will serve as a basis for future studies in this area. After publication, the digital records of the data were deleted to ensure confidentiality is maintained. The primary investigator has no conflict of interest.

CHAPTER FOUR: RESULTS

4.1 Introduction

A total of 59 patients fulfilled the inclusion criteria and had both eyes were examined for ocular manifestation of rheumatoid arthritis.

4.2 Demographic characteristics of the patients

The patient's age ranged from 19 years to 81 years with median = 52.0 (IQR=40 to 64)

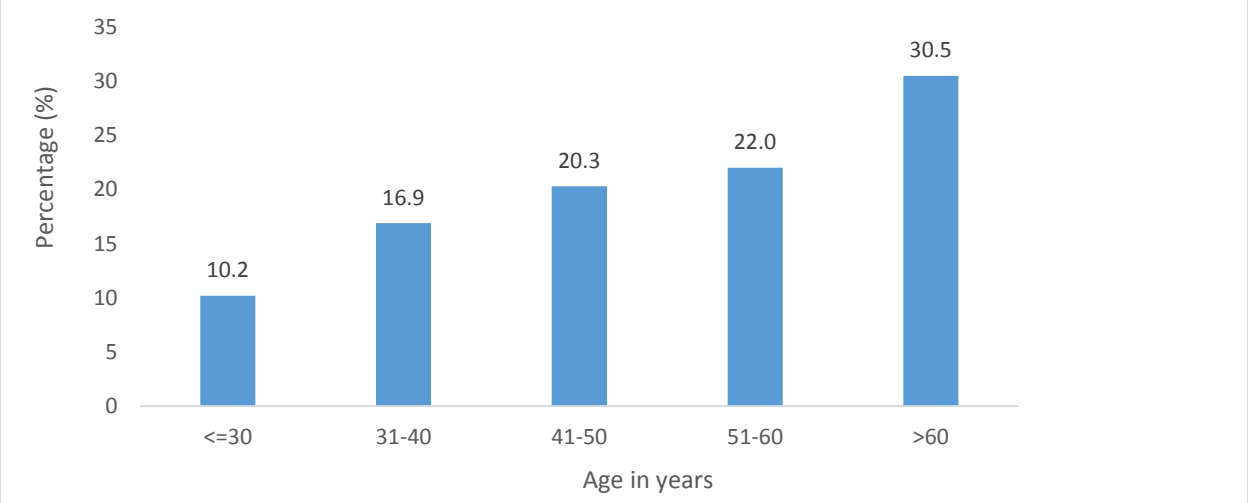

Figure 1: Distribution of patients with rheumatoid arthritis by age (n=59 patients)

As shown in Figure 2 below, females comprised of 89.8% and males 10.2% [Ratio = 1:9 (M: F)] of the total study group.

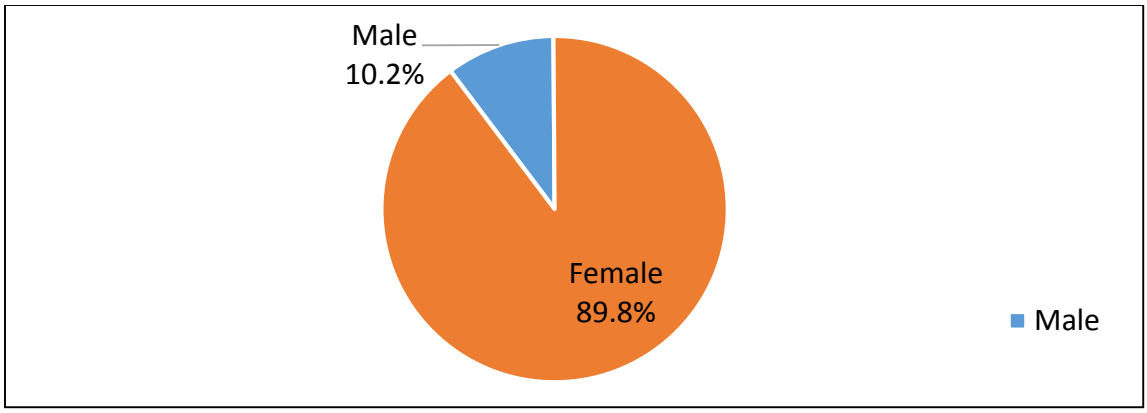

Figure 2: Distribution of rheumatoid arthritis patients by sex (n=59 patients)

4.3 Clinical characteristics related to rheumatoid arthritis

As illustrated Figure 3, 35.6% of the patients had been with symptoms for 5 to 9 years.

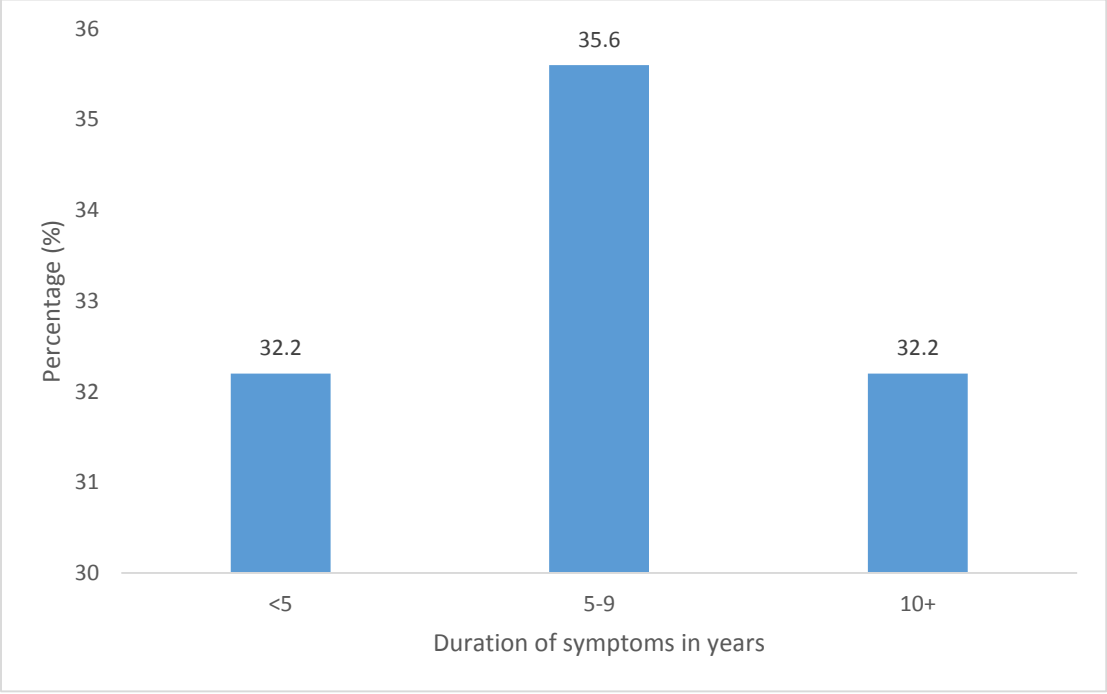

Figure 3: Duration of symptoms in rheumatoid arthritis patients (n=59 patients)

More than three-quarters (76.3%) were positive of rheumatoid factor (Table 4)

Table 4: RF Status

	Number of patients	%
Positive	45	76.3
Negative	6	10.2
Not Done	8	13.5
Total	**59**	**100**

Most patients (93.2%) were on Disease-modifying antirheumatic drugs (DMARDS) and NSAIDS (98.3%) (Figure 4).

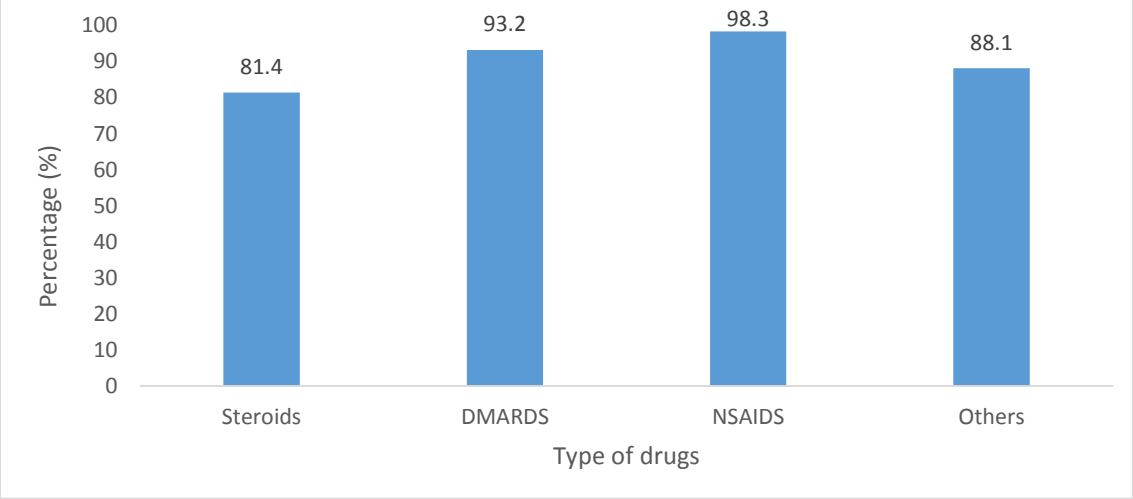

Figure 4: Medical treatment of the rheumatoid arthritis patients (n=59 patients)

NSAIDs include: Aceclofenac, Celecoxib, Etoricoxib, and Meloxicum

Steroids include: Prednisolone (oral,intra articular)

DMARDs include: HCQ (13). Methotrexate (9), Lefra (5), and Leflunomide (1)

Other drugs include: Zulu MR (1), Folic Acid (12), Omeprazole (8), Zedical (7), Paracid (2), Duzac (1), and Tramodol (1)

4.4 Ocular involvement

4.4.1 Past and Presenting Ocular History

As shown in table 5, the most common complaints at presentation were itching and blurred vision.

Table 5: Past ocular history and presenting complaints in the study population (n=59 patients)

	Past Ocular complaints		Presenting Complaints	
	No. of patients	%	No. of patients	%
Itching	34	57.6	29	49.2
Blurred Vision	26	44.1	25	42.4
Redness	25	42.4	18	30.5
Tearing	21	35.6	15	25.4
Photophobia	21	35.6	18	30.5
Foreign Body Sensation	19	32.2	17	28.8
Other*	5	8.5	4	6.8

*Other past ocular history includes: pain (2), decease near vision (2), and white discharge (1)

*Other presenting complaint include: pain (2), white discharge (1), and yellow discharge (1)

*Total is >59 because one eye can have more than one finding

4.5 Prevalence of ocular manifestations

All but 3 patients were diagnosed with at least one or more ocular manifestations. This was a prevalence of 96.6% (95% CI 91.5-100).

4.6 Types of ocular findings

A

shown in Table 6, 93.2% of the patients had dry eyes with majority (70.9%) of them being severe.

Table 6: Ocular findings in Rheumatoid arthritis (n=59 patients) 3 had normal ocular findings

Finding	**Number (%)**
Dry eye syndrome*	55 (93.2)
Cataract	13 (22.0)
Episcleritis	6 (10.2)
Retinal scar	1 (1.7)
Corneal scar	1 (1.7)

*Mild (11), Moderate (5), Severe (39)

As shown in table: 7 other ocular finding not necessarily associated with RA were found in the study population

Table 7: Other ocular findings in Rheumatoid arthritis (n=59 patients)

Finding	**Number (%)**
Blepharitis	5 (8.5)
Myopia	3 (5.1)
Glaucoma	2 (3.4)
Pinguecula	1 (1.7)
Purulent Conjunctivitis	1 (1.7)

As shown in table 8, patients with dry eyes were significantly older (mean 52.5 years), p=0.03 than those without dry eyes (mean age 36 yeas). Cataracts were also diagnosed in old patients (mean 64.4 years), p<0.00.

Table 8: Association between ocular involvement and age

Finding		**Mean (SD)**	**P value**
Dry eye syndrome	Yes	52.5 (13.9)	**0.033**
	No	36 (23.7)	
Cataract	Yes	64.4 (10.1)	**<0.001**
	No	47.7 (14.2)	
Episcleritis	Yes	51.8 (12.1)	0.942
	No	51.4 (15.5)	

Blepharitis	Yes	60 (14.1)	0.185
	No	50.6 (15.0)	

As shown in table 9, patients with more than 5 years' duration of disease had a higher prevalence of dry eye syndrome, cataract and blepharitis though it was non-significant ($p>0.05$).

Table 9: Relationship between ocular manifestations by duration of RA disease

Finding	**Duration of disease in years**	
	<5 (n=19) %	**>=5 (n=40) %**
Dry eye	17 (89.5)	38 (95.0)
Cataract	2 (10.5)	11 (27.5)
Episcleritis	2 (10.5)	4 (10.0)
Blepharitis	1 (5.3)	4 (10.0)

As shown in table 10, patients who were on steroids had significantly lower prevalence of blepharitis (4.2%) compared to 27.3% in those who were not on steroids ($p=0.040$). Also, though not statistically significant, there was a high prevalence of cataract in patients on steroids (25%)

compared to 9.1% in their counterparts ($p=0.426$). Rheumatoid factor was not significantly associated with any of the ocular manifestations ($p>0.05$).

Table 10: Relationship between ocular manifestations by steroid treatment

Finding check fonts	**Steroids**	
	Yes (n=48) %	**No** (n=11) %
Dry eye	44 (91.7)	11 (100)
Cataract	12 (25)	1 (9.1)
Episcleritis	5 (10.4)	1 (9.1)
Blepharitis	2 (4.2)	3 (27.3)

4.8 Visual Acuity

Majority (93.2%) of the patients had normal VA translating to 90.7% of all the eyes examined. Three patients (5.1%) had visual impairment and 1 (1.7%) was blind. As a proportion of total eyes studied, 5.9% were visually impaired and 3.4% blind (Table 11).

Table 11: Presenting VA of the better eye and number of eyes

VA	Number of eyes (N=118 eyes) n (%)	Presenting VA of better eye (N=59 patients) n (%)
Normal (6/6-6/18)	107 (90.7)	55 (93.2)
Visual Impairment (<6/18-6/60)	7 (5.9)	3 (5.1)
Severe Visual Impairment (<6/60-3/60)	0 (0.0)	0 (0.0)
Blind (<3/60)	4 (3.4)	1 (1.7)
Total	**118 (100.0)**	**59 (100.0)**

CHAPTER FIVE: DISCUSSION

Rheumatoid arthritis is a medical condition that occurs mostly in the elderly population who are female. Our study reviewed a population with a mean age of 51.4 years and 90% females. The duration of the disease was more than 5 years for two thirds of the population. Studies among RA patients have reported similar findings showing that the disease affects females more commonly the elderly [18], [29], [30]. A study in Iraq reported a mean age of 41.5 years with a female to male ratio of about 8 to 1 [3]. In relation to treatment, patients on DMARDS were 93% while those on steroid treatment were 81%.

Despite the high prevalence of ocular manifestations, our study population reported high visual acuity with more than 90% having normal vision with only 4 patients having visual impairment or blind. Studies such as Piper et al reported lower levels of visual acuity among RA patients with normal vision seen in 61.3% of the population and more than a third having visual impairment [29]. This difference could be attributed to the slight difference in the age of the population in the two studies. The population in our study was relatively younger.

All except two patients had ocular manifestations which was contributed more commonly by the presence of dry eyes reported in more than 90% of the RA patients. This finding was significantly higher than what is reported in the literature. A study in Bosnia reported a prevalence of ocular manifestation at 27% [20] and though dry eye syndrome is the commonest across all studies, it ranges between 15 to 70% in the literature [1], [29]. Similar findings were reported in studies in Iraq [3] and South India [18] showing dry eyes as the most common ocular manifestation in RA patients. The prevalence in our study was several

times higher than reported in studies elsewhere; in Iraq a study reported a prevalence of 27.2% [3] and two studies in India showed 22% [19] and 17.7% [22]. Piper et al reported abnormal Schirmer's test among 70.7% of the patients studied which was indicative of dry eyes in the population [29]. In our study, the patients with dry eyes were significantly older which confirms the findings by other studies that the risk increases with age among RA patients [31]. Duration of RA disease did not show significant association with occurrence of any of the ocular manifestations though the prevalence of dry eye and cataracts was higher in patients with longer duration of disease. A study among Indian patients associated dry eye syndrome with longer duration of RA disease [31].

Slightly more than one in five patients were diagnosed with cataracts. Piper et al reported similar findings with 22.7% of the RA patients diagnosed with cataracts [29]. The occurrence of cataracts in this study was found to be associated ($p<0.001$) with advancing age of the patients which may not necessarily be due to RA disease. Similar findings were reported in Piper et al where diagnosis of cataracts was associated with older age and use of steroids [29]. However, our findings did not show evidence of influence of steroids on cataracts occurrence though there was a higher prevalence of cataracts among those on steroids.

Episcleritis was also found in 10% of the RA patients. This was higher than the prevalence reported in studies elsewhere showing between 0.17 to 3.7% [13]. Mirković et al reported a prevalence of 4.3% of the patients [30]. Also, another study showed a prevalence of episcleritis at 5.1% [20].

This study found several other ocular manifestations that may not be attributed directly to the RA disease. The numbers were too small to allow for any further analysis to check their associations with the RA disease characteristics. Notably, blepharitis was less common in patients who were using steroids (4.2%) compared to those not on steroids (27.3%). This could point at the protective effect of steroids against blepharitis. In addition, ocular findings were diagnosed in patients regardless of their rheumatoid disease activity. Other studies have reported the same findings where disease activity did not have effect on the likelihood of diagnosing ocular disorders [32].

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

There is a high prevalence of ocular manifestations in RA patients. The most common ocular condition is dry eye syndrome which occurs in 9 in 10 patients. Also, cataracts contribute to the high prevalence of the ocular manifestations. Both conditions are more common in patients with advanced age. Visual impairment is an uncommon finding in RA patients despite the high prevalence of ocular manifestations in the population.

The most common ocular complain was itching, followed by blurring of vision.

6.2 Recommendations

All patients diagnosed with RA should be referred to an ophthalmologist for evaluation of ocular co-morbidities.

6.3 Limitations

It difficult to say the cataract and glaucoma are due to RA in this study because patients with RA are on high dosage of corticosteroids which can in themselves induced both cataract and/or glaucoma

DES & cataract occur more frequently with advanced age and this study found the majority of patient with DES and cataract were older.

REFERENCES

[1] C. Tehlirian and J. Bathon, "Rheumatoid arthritis, Clinical and laboratory manifestations," in *Prim on rheum dis, 13th ed.* , New York, USA, Springer science and business media, 2008, pp. 114-21.

[2] A. Young and G. Koduri, "Extra-articular manifestations and complications of rheumatoid arthritis," *Best Pract Res Clin Rheumatol.*. 21, no. 5, pp. 907-27, 2007.

[3] K. Al-Bedri, N. K. Mohammad Al-Quriashi, F. I. Gorial and H. A. Younis, "Ocular Manifestations in Rheumatoid Arthritis: A Descriptive Cross-Sectional Study from Iraq," *J of Nat Sci Res,* vol. 6, no. 3, pp. 118-123, 2016.

[4] D. Almaliotis, M. Zakalka, A. Gerofotis, K. Chatzicharalampous, M. Efstathiou, M. Daniilidis and V. Karampatakis, "Ocular Manifestations in Rheumatoid Arthritis," *Open J of Ophthal,* vol. 6, pp. 170-175, 2016.

[5] S. Patel and D. Lundy, "Ocular manifestations of autoimmune disease," *Am Fam Physician* 66, pp. 991-8, 2002.

[6] L. W. Moreland and J. R. Curtis, "Systemic nonarticular manifestations of rheumatoid arthritis: Focus on inflammatory mechanisms," *Sem in Arth and Rheum,* vol. 39, p. 132–143, 2009.

[7] V. Sahatciu-Meka, S. Rexhepi, S. Manxhuka-Kerliu and M. Rexhepi, "Extraarticular manifestations of seronegative and seropositive rheumatoid arthritis," *Bosn J Basic Med Sci.,* vol. 10, pp. 26-31., 2010.

[8] D. Fuerst, D. Tanzer and R. Smith, "Rheumatoid diseases," *Int Ophthalmol Clin.*, vol. 38, pp. 47-80, 1998.

[9] B. Dowman, R. M. Campbell, L. Zgaga, D. Adeloye and K. Y. Chan, "Estimating the burden of rheumatoid arthritis in Africa: A systematic analysis," *J of Globl Health,* . 2, no. 2, pp. 1-9, 2012.

[10] L. Tong, J. Thumboo, Y. K. Tan, T. Y. Wong and S. Albani, "The eye: A window of opportunity in rheumatoid arthritis?," *Nat Rev Rheumatoly,* . 10, p. 552–560, 2014.

[11] S. Androudi, A. Dastiridou, C. Symeonidis, L. Kump, A. Praidou, P. Brazitikos and S. Kurup, "Retinal vasculitis in rheumatic diseases: An unseen burden," *Clin Rheumatol,* vol. 32, p. 7–13, 2013.

[12] K. S. Kunert, A. S. Tisdale, M. E. Stern, J. A. Smith and I. K. Gipson, "Analysis of topical cyclosporine treatment of patients with dry eye syndrome: Effect on conjunctival lymphocytes," *Arch of Ophthalmol,* vol. 116, p. 1489–1496, 2000.

[13] M. Sainz de la Maza, N. Molina, L. A. Gonzalez-Gonzalez, P. P. Doctor, J. Tauber and C. S. Foster, "Clinical characteristics of a large cohort of patients with scleritis and episcleritis," *Ophthalmol,* vol. 119, p. 43–50, 2012.

[14] G. Stern, "Peripheral corneal disease," in *Cornea (2nd ed.)*, Philadelphia, Elsevier, 2011, p. 267–275.

[15] M. Fujita, I. Igarash and T. Kurai, "Correlation between dry eye and rheumatoid arthritis activity," *Am J Ophthalmol,* vol. 140, p. 808, 2005.

[16] J. Sims, "Scleritis: Presentations, disease associations and management," *Postgrad Med Journal,* . 88, p. 713–718, 2012.

[17] N. Lamba, S. Lee, H. Chaudhry and C. S. Foster, "A review of the ocular manifestations of rheumatoid arthritis," *Cogent Med* . 3, no. 1243771, pp. 1-5, 2016.

[18] C. Charanya, A. Swathi, S. Janti and R. Pandurangan, "Ocular Manifestation in Rheumatoid Arthritis Patients Presenting to Tertiary Care Hospital in South India: A Prospective Study," *Int Jof Scie St* . 3, no. 8, pp. 61-68, 2015.

[19] P. Kumar, "Ocular manifestation in Rheumatoid arthritis and Juvenile rheumatoid arthritis," *J of Kathmandu Med Col*. 2, no. 2(6), pp. 181-189., 2013.

[20] G. Zlatanović, Veselinović, D, S. Cekić, M. Zivković, J. Dorđević-Jocić and M. Zlatanović, "Ocular manifestation of rheumatoid arthritis-different forms and frequency," *Bosn J Basic Med Sci.,* vol. 10, no. 4, pp. 323-7, 2010.

[21] P. Ammapati, V. Pandian and S. Renuka, "Ocular manifestations of rheumatoid arthritis and their correlation with anti-cyclic citrullinated peptide antibodies," *Clin Ophthalmol.,* vol. 9, p. 393–397, 2015.

[22] D. Bhadoria, P. Bhadoria, K. Sundaram, A. Panda and A. Malaviya, "Ocular manifestations of rheumatoid arthritis," *J Indian Med Assoc.,* vol. 87, no. 6, pp. 134-5, 1989.

[23] C. Noche, G. Kagmeni, V. Dohvoma, A. Bella, C. Mvogo and M. Singwe-Ngandeu, "Ophthalmic Manifestations in Chronic Inflammatory Rheumatic Diseases at a Referral Hospital of Yaounde, Cameroon.," *Ocul Immunol Inflamm.* 1-6, 2016.

[24] C. Noche, M. Singwé-Ngandeu and A. Bella, "Rheumatoid polyarthritis suspected in an HIV patient with scleritis, peripheral ulcerative keratitis, and anterior uveitis," *Intl Med Case Reports J,* . 9, 19–24, 2016.

[25] W. Mathenge, "Ocular Manifestation in Patients with Rheumatoid Arthritis at Kenyatta National Hospital," University of Nairobi Postgraduate dessertation, Nairobi, 1995.

[26] Government of Kenya, "The 2009 Kenya Population and Housing Census: Kenya National Bureau of Statistics," Government Printer, Nairobi, 2010.

[27] S. Wanga and S. Lemeshow, Sample size determination in health studies. A practical manual, Ginebra: WHO, 1991.

[28] B. Bowling, Kanski's Clinical Ophthalmology: A Systematic Approach, Elsevier, 2016.

[29] Piper H, Douglas K, Treharne G, Mitton D, Haider S, Kitas G. Prevalence and predictors of ocular manifestations of RA: is there a need for routine screening? Musculo Care. 2007; 5(2):102-117

[30] Mirković M., Jakšić B., Vukša D., Stamenković D., Bulajić S., Petković Z., Elek S. Ocular manifestations in patients with rheumatoid arthritis. Praxis medica. 2011; 39 (1-2): 131-134.

[31] Santosh K, Dhir V, Singh S, Sood A, Gupta A, Sharma A, Sharma, S. Prevalence of secondary Sjogren's syndrome in Indian patients with rheumatoid arthritis: a single-center study. Int J of Rheum Dis 2017; 20: 870–874.

[32] *El-Badawy MA, El-Mahdi AR, Samia El Rehem MA, Ebeid WM, El-Kitkat RS, Abdelaziz DM.* Evaluation of disease activity markers in relation to dry eye disease in patients with rheumatoid arthritis. Egyptian Rheumatol and Rehab. 2017; 44(3):111-117.

APPENDICES

Appendix I: Consent Information

Introduction

My name is Dr. Aja Paul Kuol. I am a post graduate student in the Department of Ophthalmology at University of Nairobi.

I am conducting a study on: Ocular Manifestation in Rheumatoid Arthritis Patient Attending the Rheumatology Clinic at the Kenyatta National Hospital

Purpose of the Study

To determine the ocular manifestation in rheumatoid arthritis patient attending the rheumatology clinic at Kenyatta National Hospital.

Basis of Participation

Your participation will be voluntary. You are free to withdraw at any time during the course of the study period. Your refusal to participate or withdrawal at any time during the study period will not in any way affect the quality of your treatment.

Confidentiality

All information obtained in the study will be treated with utmost confidentiality.

I shall NOT use your name in any of my reports.

Benefits

The results of this study may be published in a medical book or journal or for teaching purposes and will be given to the community for better understanding of this topic. You will be given a copy of your visual field result for your medical records.

Risk and Discomfort

Any examination process that will be conducted by the researcher will cause no damage to the participant.

Request for Information

You may ask more questions about the study at any time or at this moment. You will be informed of any significant findings.

You may contact Dr. Aja Paul Kuol on 0728434037 or Dr. Sheila Marco (UON, Department of Ophthalmology) or Prof. Jefitha Karimurio (UON, Department of Ophthalmology) or KNH/UON Ethical Review Committee Secretariat P.O. Box 20723 – 00202, Nairobi, Telephone Number: +254 2726300 Ext. 44102 and email address uonknherc@uonbi.ac.ke

Supervisor's contacts:

Dr.Sheila Marco (department of ophthalmology - UON) (sheilamarco@yahoo.co.uk)

Professor, Jefitha Karimurio (Department of ophthalmology-UON) (jkarimurio@gmail.com)

Appendix II: Consent

Having read this consent form, all my questions have been answered; my signature below indicates my willingness to participate in this study and my authorization to use and share with fathers.

I …… the (Patient/Guardian) of …… after reading and having the study purpose explained to me by Dr. Aja Paul Kuol, do hereby give informed consent to participate in the study: **ocular manifestations in rheumatoid arthritis patients attending rheumatology clinic at KNH**

Signed ……. Date ……

Thumb Print …… Date ……

I confirm that I have explained to the patient the above statement.

Signature of questionnaire Investigator

……..

Dr. Aja Paul Kuol

Phone No.: +254 0728434037

Appendix III: Maelezo Ya Kibali Na Fomu Ya Kibali

Utangulizi

Jina langu ni Dk. Aja Paul Kuol. Mimi ni mwanafunzi wa shahada katika Idara ya Ophthalmology katika Chuo Kikuu cha Nairobi.

Ninafanya utafiti juu ya: Maonyesho ya Ocular katika Hospitali ya Mifupa ya Arthritis Matibabu Kuhudhuria Kliniki ya Rheumatology katika Hospitali ya Taifa ya Kenyatta

Sababu ya Utafiti

Kuamua udhihirisho wa macho katika mgonjwa wa arthritis ya rheumatoid kuhudhuria kliniki ya rheumatology katika Hospitali ya Taifa ya Kenyatta.

Msingi wa Kushiriki

Ushiriki wako utakuwa hiari. Wewe ni huru kujiondoa wakati wowote wakati wa kipindi cha kujifunza. Kukataa kwako kuhusika au kuondoa wakati wowote wakati wa kujifunza haitaathiri ubora wa matibabu yako kwa njia yoyote.

Usiri

Taarifa zote zilizopatikana katika utafiti zitashughulikiwa kwa usiri mkubwa.

Sitatumia jina lako katika ripoti zangu yoyote.

Faida

Matokeo ya utafiti huu yanaweza kuchapishwa katika kitabu cha matibabu au jarida au kwa madhumuni ya kufundisha na itapewa kwa jumuiya kwa kuelewa vizuri kwa mada hii. Utapewa nakala ya matokeo yako ya kuona kwa kumbukumbu zako za matibabu.

Hatari na Usumbufu

Mchakato wowote wa uchunguzi ambao utafanyika na mtafiti hautaweza kumiza mshiriki.

Ombi la Taarifa

Unaweza kuuliza maswali zaidi kuhusu utafiti wakati wowote au wakati huu. Utafahimishwa kama kuna matokeo yoyote muhimu.

Unaweza kuwasiliana na Dk. Aja Paul Kuol kwa nambari ya simu 0728434037 ama Dk. Sheila Marco (UON, Idara ya Ophthalmology) or Prof. Jefitha Karimurio (UON, Idara ya Ophthalmology) ama KNH/UON Sekretarieti ya Kamati ya Ukaguzi wa Maadili, Sanduku la Poasta 20723 – 00202, Nairobi, Namabari ya Simu: +254 2726300 Ext. 44102 na barua pepe uonknh_erc@uonbi.ac.ke

Kibali

Baada ya kusoma fomu hii ya idhini, maswali yangu yote yamejibiwa, saini yangu hapa chini inaonyesha nia yangu ya kushiriki katika utafiti huu na idhini yangu ya kutumia na kushirikiana na wengine.

Mimi..... (Mgonjwa / Mlezi) wa ..... baada ya kusoma na kuwa na madhumuni yaliyoelezwa na Dk. Aja Paulo Kuol, na kutoa idhini ya kushiriki katika utafiti: **Maonyesho ya Ocular katika Mifupa ya Arthritis ya Rumumatiki Kuhudhuria Kliniki ya Rheumatology katika Hospitali ya Taifa ya Kenyatta**

Ilisainiwa _____ Tarehe _____

Kuchapa Thumb _____ Tarehe _____

Ninathibitisha kwamba nimemwelezea mgonjwa taarifa hiyo hapo juu.

Saini ya Mpelelezi Mkuu: _____

Dk Aja Paul Kuol

Nambari ya Simu: +254 0728434037

Appendix IV: Questionnaire

SECTION A: SOCIO-DEMOGRAPHIC DATA

1. **Patient Code No.: _____**
2. **Age (yrs.): _____**
3. **Sex:** ☐ Male (1) ☐ Female (2)

SECTION B: RHEUMATOID ARTHRITIS HISTORY

4. **Duration of Symptoms _____**

SECTION C: TREATMENT

DRUG	**DURATION**
NSAIDs	
Steroids	
DMARDs	
Others	

SECTION D: PAST OCULAR HISTORY

☐ Blurred Vision(1)
☐ Foreign body sensation (2)
☐ Itching (3)
☐ Tearing (4)
☐ Redness (5)
☐ Photophobia (6)
Other _____

SECTION E: PRESENTING COMPLAINTS

☐ Blurred Vision(1)
☐ Foreign body sensation (2)
☐ Itching (3)
☐ Tearing (4)
☐ Redness (5)
☐ Photophobia (6)
Other _____

SECTION F: OCULAR EXAMINATION

RE	**LE**
Presenting V/A	Presenting V/A
_____	_____
Pinhole/BCVA	Pinhole/BCVA
_____	_____
IOP	IOP
_____	_____
Lids	Lids
_____	_____
Conjunctiva	Conjunctiva
_____	_____
Episclera	Episclera
_____	_____
Cornea	Cornea
_____	_____
Anterior Chamber	Anterior Chamber
_____	_____
Iris	Iris
_____	_____
Pupil	Pupil
_____	_____
Lens	Lens
_____	_____
Vitreous	Vitreous
_____	_____
Optic Disc	Optic Disc
_____	_____
Macula	Macula
_____	_____

Retina	Retina
_____	_____
Tear meniscus	Tear meniscus
_____	_____
Schirmer's Test 2 _____	Schirmer's Test2_____
BUT_____	BUT_____
Photograph No. _____	Photograph No. _____
Diagnosis _____	Diagnosis_____

Appendix V: The 2010 ACR-EULAR Classification Criteria for Rheumatoid Arthritis

	Score
Target population (Who should be tested?): Patients who 1. have at least 1 joint with definite clinical synovitis (swelling)* 2. with the synovitis not better explained by another disease†	
Classification criteria for RA (score-based algorithm: add score of categories A - D; a score of ≥ 6l10 is needed for classification of a patient as having definite RA)	
A. Joint involvement§	
1 large joint¶	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)#	2
4-10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)**	5
B. Serology (at least 1 test result is needed for classification) ††	
Negative RF and negative ACPA	0
Low-positive RF or low-positive ACPA	2
High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification) ‡‡	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
D. Duration of symptoms§§	
<6 weeks	0
•≥ 6 weeks	1

* The criteria are aimed at classification of newly presenting patients. In addition, patients with erosive disease typical of rheumatoid arthritis (RA) with a history compatible with

prior fulfillment of the 2010 criteria should be classified as having RA. Patients with longstanding disease, including those whose disease is inactive (with or without treatment) who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA.

† Differential diagnoses vary among patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout. If it is unclear about the relevant differential diagnoses to consider, an expert rheumatologist should be consulted.

‡ Although patients with a score of <6/10 are not classifiable as having RA, their status can be reassessed and the criteria might be fulfilled cumulatively over time.

§ Joint involvement refers to any *swollen* or *tender* joint on examination, which may be confirmed by imaging evidence of synovitis. Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are *excluded from assessment*. Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement.

¶ "Large joints" refers to shoulders, elbows, hips, knees, and ankles.

"Small joints" refers to the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists.

** In this category, at least 1 of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g., temporomandibular, acromioclavicular, sternoclavicular, etc.).

†† Negative refers to IU values that are less than or equal to the upper limit of normal (ULN) for the laboratory and assay; low-positive refers to IU values that are higher than the-positive refers to IU values that are >3 times the ULN for the laboratory and assay. Where rheumatoid factor (RF) information is only available as positive or negative, a

positive result should be scored as low-positive for RF. ACPA = anti-citrullinated protein antibody.

‡‡ Normal/abnormal is determined by local laboratory standards. CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

Duration of symptoms refers to patient self-report of the duration of signs or symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.

Appendix VI: Study time frame

Activities	APR 2017	MAY 2017	JUN 2017	JUL 2017	AUG 2017	SEP 2017	OCT 2017	NOV 2017	DEC 2017	JAN 2018	FEB 2018	MAR 2018	APR 2018	MAY 2018	JUNE 2018	JULY 2018	AUGUST 2018
Proposal Development																	
ERC Approval																	
Data Collection																	
Data Analysis																	
Report Writing																	
Dissemination of Findings																	

Appendix VII: Budget

MMed Thesis Budget **TITLE: OCULAR MANIFESTATIONS IN RHEUMATOID ARTHRITIS PATIENTS ATTENDING THE RHEUMATOLOGY CLINIC AT THE KENYATTA NATIONAL HOSPITAL** **Principal Investigator: Aja Paul Kuol**			
Item	Quantity	Unit Cost	Total Cost
Proposal/Ethical approval and ministry of Education approval			
Proposal writing & printing	6 copies	Ksh 10 per page	4000
Binding Proposal	6 copies	100	600
Ethics	1	2000	2000
Airtime		Ksh. 3 per minute	2000
		Subtotal	**8600**
Data Collection			
Typing and Printing of Questionnaires		60 per copy	300
Photocopy of questionnaires		18 per copy	10000
Stationary –pens, erasers,etc.			2000
Flash Disc 16GB HP	1	4500	4500
Box files for filing questionnaires	10	450 each	4500
		Subtotal	**21300**
Contracted services			
Statistician	1		50000
Research assistant	1		25000
		Subtotal	**75000**
Printing costs and binding of Final book			
Finished book printing (120 pages approximately)	8 copies- 100 pages	Ksh 10 per page	8000
	8 copies- coloured20 pages	Ksh 30 per page	4800
Binding Finished book	2 copies- marking	100 per book	200
	8 final copy (black cover)	300	2400
		Subtotal	**15400**
TOTAL BUDGET			**120300**

Appendix VIII: Ethical approval

UNIVERSITY OF NAIROBI
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Ref: KNH-ERC/ Mod&SAE/25

31st January 2018

Dr. Aja Paul Kuol
Reg. No.H58/63241/2013
Dept.of Ophthalmology
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Kuol

Re: Approval for addition of a Rheumatologist - study titled, "Ocular manifestations in Rheumatoid Arthritis Patients attending the Rheumatology Clinic at the Kenyatta National Hospital (P644/11/2017)

Refer to your communication dated 24th January 2018.

The KNH- UoN ERC has reviewed and **approved** inclusion of Prof. George Oyoo, Consultant Physician and Rheumatologist, Dept.of Clinical Medicine & Therapeutics, UoN as an additional supervisor in the above study.

The revised document has been amended accordingly.

Yours sincerely,

PROF.M.L. CHINDIA
SECRETARY, KNH-UON ERC

c.c. The Principal, College of Health Sciences, UoN
The Director CS, KNH
The Chairperson, KNH-UON ERC
The Dean, School of Medicine, UoN
The Chair, Dept.of Ophthalmology, UoN
Supervisors: Dr.Sheila Marco, Prof.Jefitha Karimurio, Prof. George Oyoo

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