MBARARA UNIVERSITY OF SCIENCE AND TECHNOLOGY

FACULTY OF MEDICINEDEPARTMENT OF OPHTHALMOLOGY

VALIDITYOF McMONNIESQUESTIONNAIRE IN DIAGNOSING AND GRADING DRY EYE SYNDROMEAMONG PATIENTSAGED40 YEARS AND ABOVE ATTENDING RUHARO EYE CENTER, UGANDA

BY

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DECLARATION

I, Gladys Atto hereby declare that the work I have presented in this dissertation in the partial fulfillment of the requirement for the ward of the degree of Masters of Medicine in Ophthalmology of Mbarara University of science and technology is my own original study at Ruharo Eye Center except where otherwise acknowledged. It has not been submitted to any other university or institute for any other award whatsoever.

Dr Gladys Atto

Signature…… Date……

SUPERVISORS' APPROVAL

The research work culminating into this dissertation was conducted under my guidance and supervision.

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DEDICATION

I dedicate this work to my parents: Lucy Adong and Milton Nyeko and siblings: Rita Adoch, Ronald Acire and Emmanuel Okello.

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I thank the almighty God for the good health and protection throughout this training.

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ABBREVIATIONS AND ACRONYMS

DES: Dry Eye Syndrome

DEWS: Dry Eye Workshop

MUST: Mbarara University of Science and Technology

MURHEC: Mbarara University and Referral Hospital Eye Centre

NMS: National Medical Stores

OPD: Out Patient Department

TBUT: Tear Break Up Time

RA: Rheumatoid Arthritis

RB: rose Bengal

SLE: Systemic Lupus Erythematosis

SS: Sjogren syndrome

MGD: Meibomian Gland Disease

MQ: McMonnies Questionnaire

KCS: Keratoconjunctivitis Sicca

LASIK: Laser-Assisted in Situ Keratomileusis.

REC: Ruharo Eye Centre

COECSA: College of East, Central and Southern Africa.

JOECSA: Journal of East, Central and Southern Africa.

DEFINITION OF TERMS

Dry Eye Syndrome occurs when there is reduced tear volume or inadequate function thus causing an unstable tear film and ocular surface disease. The tear film is made up of three layers:

- The Lipid layer which is secreted by the meibomian glands is the top layer and prevents evaporation of the aqueous layer, maintains the thickness of the tear film, and allows it to spread evenly. Deficiency of this layer leads to evaporative Dry Eye Syndrome.
- The Aqueous layer which is secreted by the lacrimal glands is the middle layer and makes up 90% of the tear film. It provides oxygen and nutrients to the cornea, has some antibacterial activity and washes away debris.
- The inner mucous layer is secreted by the goblet cells in the conjunctiva and its deficiency may be a due to both aqueous deficiency and evaporative dry eye.

Sjogren Syndrome is a disease with autoimmune inflammation and destruction of lacrimal and salivary glands. The condition can exist in isolation and so is classified as primary. The secondary classification is when it is associated with other diseases like rheumatoid arthritis, SLE, systemic sclerosis, mixed connective tissue disease, primary biliary cirrhosis, chronic active hepatitis and myasthenia gravis. Primary Sjogren syndrome affects females more than males.

ABSTRACT

Background: The international Dry Eye Workshop 2007 (DEWS) defined dry eye syndrome (DES) as "a multifactorial disease of the tear and ocular surface that results 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"(DEWS, 2007a). DES is very common, affecting a significant percentage of the population, especially those older than 40 years with prevalence estimates ranging from approximately 10-30% of the population in the United States (Foster, 2015) to 27.5% (Lee, 2002) in rural Indonesia and 18.4% (Sahai, 2005) in India.In Uganda, DES is common but there is no national prevalence data available. Hospital data at Ruharo Eye Center shows that about 672 patients out of the 7726 adults who presented for eye care services in 2015 were diagnosed with DES and of these, 416 were 40 years and above (unpublished).The McMonnies questionnaire is among the earliest and most widely used screening instruments for DES and it was found to be a useful tool in detecting the presence of dry eye disease and those at risk of developing the disease(Erickson, 2002)In our current practice, diagnosis of DES is mainly symptomatic leaving many asymptomatic patients untreated which calls for the need for an easy to use and inexpensive screening tool (Erickson, 2002).

Aim: To determine the sensitivity and specificity of McMonnies questionnaire in diagnosing and grading the severity of DESamong patients who are 40 years and above attending REC.

Design and methods: This was a cross-sectional hospital-based study conducted during the months of September and December 2017. We included both males (76) and females (91) who were 40 years and above using convenient sampling. All participants were screened for DES using MQ after whichassessment for the signs of DES using Schirmer I, TBUT and Rose Bengal tests were done. We entered data into Excel and exported into Stata 13 for analysis.

Results: A total of 167 patients were enrolled and 91 (54.49%) were females. The female to male ratio was 1.2:1. The median age of the patients was 63 years (IQR 54-72 range 40-94). Most of the patients underwent some form of education 111 (66.47) while the remaining 56 (33.35%) had no formal education. The majority, 124 (74.25) were peasants. The median Schirmer I and TBUT scores were 14 mm (IQR 5-22 range of 1-35) and 6.67 seconds (IQR 3.33-17, range of 1-34.33) respectively and that of MQ was 12 (IQR 9-17 range of 2-27).The proportion of patients with DES was 68% as determined by the composite score andthe biggest proportion, 111 (66.47%) had mild/moderate DES, 54 (32.34%) were normal while 2 (1.19%) had severe DES. The sensitivity and specificity of McMonnies questionnaire in diagnosing DES were 81.6% (95% CI, 73.2 - 88.2) and 39.6% (95% CI, 26.5 - 54) respectively and for grading DES severity were 61.1% and 18.6% for normal; 63.6% and 40.4% for mild/moderate and 50% and87.9% for severe as shown below.

Conclusion: The proportion of patients with DES was high, (68%). The MQ proved to be a good screening tool with a sensitivity and specificity of 81.3% and 36.9% respectively; however, it yielded poor results when it came to grading the severity of DES. We therefore recommend routine screening of patients in this age group for DES using MQ but advice against using it as a grading tool.

CHAPTER ONE: INTRODUCTION

1.1 Background

The international Dry Eye Workshop 2007 (DEWS) defined dry eye syndrome (DES) as a multifactorial disease of the tear and ocular surface that results 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(DEWS, 2007a). Dry Eye Syndrome (DES) is very common, affecting a significant percentage of the population, especially those older than 40 years with prevalence estimates ranging from approximately 10-30% of the population in the United States (Foster, 2015) to 27.5% (Lee, 2002) in rural Indonesia and 18.4% (Sahai, 2005) in India. In Uganda, DES is common but there is no national prevalence data available. Hospital data at Ruharo Eye Center shows that about 672 patients out of the 7726 adults who presented for eye care services in 2015were diagnosed with DES and of these, 416 were 40 years and above (unpublished).

Dry eye has been called the back pain of eye care, one of those nebulous conditions of many, often unknown etiologies that is a source of great frustration to patients and their eye care providers (Moss et al., 2000).In the United States alone, approximately 7–10 million Americans require artificial tear preparations, with consumers spending over US $100 million/year (Lee, 2002). Symptoms are often nonspecific and include: redness, burning, stinging,foreign body sensation, pruritus and photophobia; more or less pronounced conjunctival redness and damage to the ocular surface with punctate epithelial erosions (superficial punctate keratitis) are also typical in dry eye.(EM, 2015a)

A variety of diagnostic tests are in common clinical usage such as TBUT, Schirmer, tear osmolarity, ocular surface stains but there is no consensus as to which combination of tests should be used to define the disease either in the clinic or for the purposes of a research protocol (DEWS, 2007b). Practitioners sometimes make use of dry eye questionnaires to identify patients at risk for dry eyes (Erickson, 2002).The McMonnies questionnaire (MQ) is among the earliest and most widely used screening instruments for DES and it was found to be a useful tool in detecting the presence of dry eye disease and those at risk of developing the disease(Erickson, 2002)

In as far as management is concerned, a number of treatments of varying efficacy also exist, but there is no known cure as yet for DES (MA, 1998); multi-interventional approach commonly involves using tear supplementation, steroids, eyelid hygiene, and omega-3 essential fatty acids(Javadi, 2011). Artificial tear supplements, which vary widely in their composition, serve to keep the ocular surface lubricated and help relieve patient discomfort(Javadi, 2011). Early detection and aggressive treatment however, helps to prevent serious complications like corneal ulcers and scarring that would result in poor vision(Foster, 2015)**.**In our current practice, diagnosis of DES is mainly symptomatic leaving many asymptomatic patients untreated which calls for the need for an easy to use and inexpensive screening tool (Erickson, 2002).

1.2 Problem Statement

Dry Eye Syndrome is considered one of the commonest eye diseases though one which is rarely approached with enough gravity given the impact the disease can have on the people who live with it and the fact that its management is also approached somewhat subjectively (Lemp, 2007).In the year 2015 alone, a review of records at REC showed that about 672 out of7725 patients had been diagnosed with DES (unpublished).However, this figure is most likely to be an underestimate of the magnitude of DES in this Eye Center given the fact that dry eye is not actively sought for in the out patients**..**

Secondly, in Ruharo Eye Center, where over a hundred patients are seen per day, and considering the low ophthalmologist to patient ratio, patients are prone to spending long hours in the hospital if all the clinical tests for dry eye are to be done for every patient. In addition, clinicians would not be motivated to carry an array of tests to diagnose DES as that would increase the work load to their already stretched hours. Therefore identification of a fast, inexpensive, low-burden, non-invasive and easy-to-use tool for identifying patients at risk of having DES such as the MQ would be very helpful.

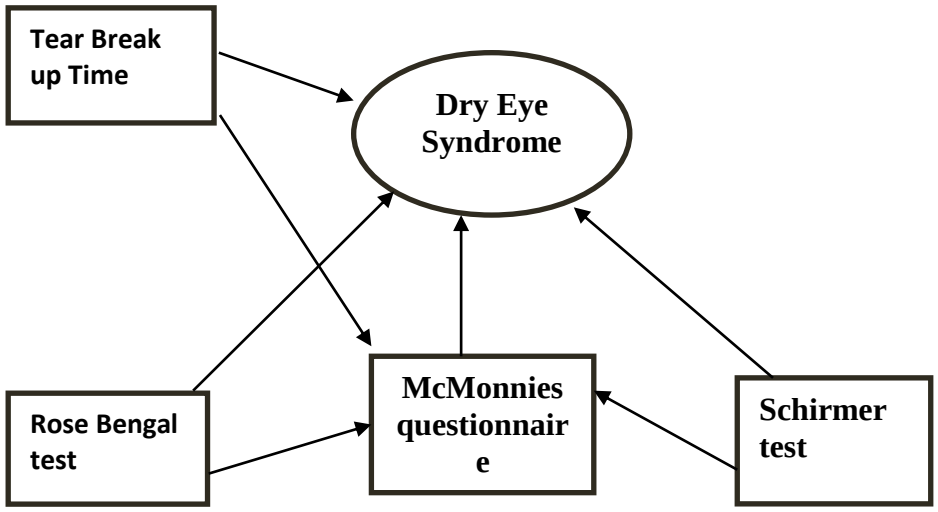
Also, considering the fact that most studies(McMonnies, 1998, Nichols, 2004b)evaluating the reliability and validity of MQfocused mostlyon non-African populations,it is anticipated that variations in the diagnostic efficacy are likely to occur when applying this tool to an African cohort. This study will therefore aim at investigating the sensitivity and specificity of MQ as a screening and grading tool for dry eye among patients who are 40 years and above attending

outpatients of Ruharo Eye Centre (REC) and also provide information on the magnitude of the DES in a referral Eye Centre.

1.3 Justification

The results of the study willhelp to identify a cheap, inexpensive and easy to use screening tool that will ensure that no patient who walks into the Eye Centre with DES leaves undiagnosed and also provide a true picture of the magnitude of DES at a referral Eye Center, an information which will be quite useful for research and clinical purposes since no national prevalence data on DES is available. Also the information obtained from the study will be shared with other eye care facilities to encourage adequate screening for patients with DES.

Figure 1: Conceptual framework



1.4 Conceptual framework Narrative

The above diagram shows how the various clinical tests correlate with McMonnies questionnaire which is a subjective test to influence the outcome variable which is Dry Eye Syndrome. Tear Break Up Time, Schirmer test and Rose Bengal tests are clinical tests for DES while McMonnies questionnaire only screens for patients who are suspected to be having DES before any of the clinical tests are performed. Therefore, if a patient tests positive with any of these tests, a diagnosis of DES is made irrespective of whether they tested positive or negative with McMonnies questionnaire.

1.5 Research Questions:

1. What proportion of patients aged 40 years and above attending REC have DES?
2. What is the sensitivity and specificity of McMonnies questionnaireas a screening tool for DES among patients who are 40 years and above attending REC?
3. What is the sensitivity and specificity of McMonnies questionnaireas a grading tool for DES severityamong patients who are 40 years and above attending REC?

1.6Objectives

1.61 General objective

To assessthesensitivity and specificity of McMonnies questionnaire as a screening and grading tool for Dry Eye Syndromeamong patients who are 40 years and above attending Ruharo Eye Centre (REC), South western Uganda.

1.62 Specific Objectives

1. To determine the proportion of patients who are 40 years and above with DES attending REC.
2. To determine the sensitivity and specificity of McMonnies questionnaire as a screening tool for DES compared toa reference composite score of Tear Break UpTime (TBUT) and Schirmer I tests among patients who are 40 years and above attending REC.
3. To determine the sensitivity and specificity ofMcMonnies questionnaire as a grading tool for severity of DES among patients who are 40 years and above attending REC compared to a composite disease severity score of Schirmer I, TBUT and Rose Bengal tests.

CHAPTER TWO: LITERATURE REVIEW

2.1 Background

The international Dry Eye Workshop 2007 (DEWS) defined dry eye syndrome (DES) as "a multifactorial disease of the tear and ocular surface that results 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"(DEWS, 2007a). It has been recognized as resulting from a disturbance of the Lacrimal Functional Unit (LFU), an integrated system comprising the lacrimal glands, ocular surface (cornea, conjunctiva and meibomian glands) and lids, and the sensory and motor nerves that connect them(Stern, 1998). Disease or damage to any component of the LFU can destabilize the tear film and lead to ocular surface disease that expresses itself as dry eye(DEWS, 2007a).

DES commonly presents as; itching, burning, a sense of dryness, foreign body sensation, ocular pain, photophobia, blurred vision, eye fatigue(Merck Manual, 2014)**.** DES is associated with a long list of causes which can be divided into primary and secondary. Dry eye may develop secondary to inflammatory disease (e.g. vascular, allergic), environmental conditions (e.g. allergens, cigarette smoke, dry climate), hormonal imbalance (e.g. perimenopausal women and patients under hormone replacement therapy), and contact lens wear. Systemic disorders, such as diabetes mellitus, thyroid disease, rheumatoid arthritis and systemic lupus erythematosus can also lead to dry eye as well as neurotrophic deficiency and previous eye surgery (such as corneal transplantation, extracapsular cataract)(Javadi, 2011).

2.2 Classification

DES may be divided into "aqueous-deficient" which is dry eye due to reduced tear production and is estimated to account for 10% of the cases. The second part is "hyperevaporative" which is dry eye due to increased evaporation of the tear film. This is usually due to the dysfunction of the meibomian glands. The mixed type (hyperevaporative and aqueous-deficient) accounts for more than 80% of cases (EM, 2015c)**.**

Aqueous-deficient dry eye can be subdivided into non-Sjogren syndrome and Sjogren syndrome (SS). This is an autoimmune disease often associated with infiltration into the lacrimal and salivary glands through the lymph system. Evaporative dry eye can also be further subdivided into meibomian gland disease (MGD) and exposure-related dry eye (Javadi, 2011).

A three part classification has also been developed: the first part which is etiopathogenic shows the numerous, causes of dry eye. The second is mechanistic and illustrates how the individual causes of dry eye may act through a common pathway. This classification shows that any type of dry eye may interact with or exacerbate other forms resulting in a vicious circle. The third part is based on the severity of the disease, which is often used to provide a basis for proper management(DEWS, 2007a).

2.3Prevalence of DES

DES is considered one of the commonest eye diseases though one which is rarely approached with enough gravity given the impact the disease can have on the people who live with it and given the fact its management is also approached somewhat subjectively (Lemp, 2007). Worldwide, dry eye has been estimated to affect 5–30% of the population (DEWS, 2007b). The prevalence of dry eye in the US, Australia, and Asia in 73,899 patients from eight epidemiologic studies, ranged from 8 to 34% (DEWS, 2007b). The vast majority of these patients were older than 40 years of age. Increasing age is considered a known risk factor for developing dry eye (DEWS, 2007b). In Africa, an unpublished study carried out in Juba, South Sudan identified DES as the commonest ocular surface disease with a prevalence of 199 (36.9%) (Lawrence, 2014) While In Kenyatta National Referral hospital, the Prevalence of DES among diabetic patients alone was found to be 49.8% , with more females (M:F 1:2.2) and the prevalence also increased with age (Ogundo, 2015).

Various studies have shown that the prevalence of DES is highest amongst the older population, these include; one carried out in Yongin, Korea where the adjusted prevalence of dry eye was as high as (33.2%) in people aged 65 years or older (Liu, 2014)and another done in Wisconsin which found the incidence to be 21.6% over a 10 year period amongst patients aged 43 years to 86 years (Moss et al., 2000).

The prevalence of DES was also found to be 27.5% in Indonesia (Lee et al., 2002) and 18.4% in India (Sahai, 2005) , however, when adjusted for age, dry eye prevalence was found to be maximum in those above 70 years of age (36.1%) followed by the age group 31-40 years (20%) and was also found to be significantly higher in females with a prevalence of 22.8% than in males who had a prevalence of 14.9% (Sahai, 2005). Some studies have found no correlation between dry eye and age or sex (Javadi, 2011). In as far as environmental factors are concerned,

a retrospective study found a low incidence of overt dry eye (2%) after LASIK surgery (Azuma, 2014).In Uganda, there is no national prevalence data on DES, however, our study found a high prevalence of 68% with no significant difference in males and females

2.4 Screening for DES

Despite the fact that there is no globally accepted guideline for diagnosing DES, the following tests are or a combination thereof in common usage;

2.41 The McMonnies Questionnaire (MQ)

The McMonnies dry eye questionnaire is considered a 'gold standard' for examining dry eye symptoms in disease conditions(Erickson et al, 2002). It is among the earliest and most widely used screening instruments for dry eye syndromes with a sensitivity ranging between 87% and 98% and a specificity of between 87% and 97% (Nichols et al, 2004b). It has 14 questions focusing on symptoms and risk factors for dry eye. Some of the questions include age, gender, dry eye symptoms, previous dry eye treatments, secondary symptoms (associated with environmental stimuli), medical conditions associated with dry eye syndrome, dryness of mucous membranes and medication use (Nichols, 2004b). The theoretical basis of this questionnaire is that it may be used as a screening instrument to identify patients who warrant subsequent clinical examination procedures (McMonnies, 1987a). In one study, McMonnies score proved to be a good screening tool with a sensitivity of 97.7% and it was also found to be an effective tool in screening dry eye when correlated with dry eye clinical tests (Aditya, 2013).The questionnaire helps detect the presence of dry eye disease and those at risk of developing the disease (Gothwal, 2010). Gothwal and associates agree that MQ is an effective screening instrument but question its role as a measure of disease severity (Gothwal, 2010). MQ has also been found to be a better tool in predicting contact lens induced dry eye than the ocular surface index (Michel, 2009).

Nichols et al (2004b) found that the questionnaire demonstrates fair reliability and validity as a patient-reported instrument for use in patient care and clinical studies of patients with dry eye disease. Erickson et al (2002) shared these sentiments by stating that the MQ is a statistically reliable instrument and practitioners can feel confident that the questionnaire provides a consistent and repeatable measurement.

A Multicenter Analysis carried out in China to evaluate the diagnostic Performance of MQ as a Screening tool for dry eye also found the tool to have fine validity and reported that the scores not only differed significantly between the dry eye and control groups but also strongly correlated with the results of TBUT and Schirmer I test (Yuxin, 2016) in contrast to Some prevalence studies (Hay, 1998, Schein, 1999) which indicated poor correlations between dry eye symptoms and objective clinical tests. Bhatnaga et al (2015) in their study concluded that Subjective assessment plays an important role in diagnosing dry eye disease and they also found a strong correlation between MQ and Schirmer test, TBUT, Rose Bengal staining and Lissamine green staining in normal as well as marginal and pathological dry eye.

2.42 Schirmer test

The Schirmer test was first described in 1903 by Schirmer and is still one of the most commonly used measures of aqueous tear production (Graefes, 1903). Since then, variations of the Schirmer test have been created. In relation to assessment of tear quantity, the Schirmer test still remains the "gold standard" and it is commonly accepted that 5 mm of wetting denotes tear deficiency when the test is performed without anesthesia (Murat, 2005). A comparable diagnostic cut-off value has not been agreed on for the Schirmer test with anesthesia. The Schirmer test with anesthesia, also referred to as a basic secretion test, has been reported to give more variable results than the Schirmer test done without anesthesia (Clinch, 1983). The Schirmer I test measures total tear secretion, including reflex and basal tears and has been shown to have a high sensitivity (85% and 83% respectively), however it has also been shown to give variable results (Clinch, 1983). In Schirmer 1 test, the Schirmer strips are inserted into the temporal lower conjunctival sac, without instilling drops of local anesthesia while avoiding contact with the cornea, and the length of wetting strips is recorded in millimeters after 5 minutes (Maya, 2014). Normal mean test values range from 8 mm to 33 mm, but an accepted normal value is greater than 10 mm (Shapiro, 1979, Jordan, 1980). In a study comparing Schirmer I with and without anesthesia, with anesthesia was found to be more objective and reliable in terms of diagnosing dry eyes than without anesthesia (Li, 2012). However, if the clinician chooses to perform the Schirmer I test without anesthesia, it has been found that patients with eyes closed have a more reliable result because the eyelid margin and eyelash stimulation can alter the tear turnover rate (Li, 2012). The Schirmer test was found to be more reproducible in more advanced

cases of dry eye disease (Nichols, 2004a) and also more reliable in diagnosing dry eye (Rahman, 2007). One large study conducted in Taiwan (N=459), agreed with the above finding because their study results indicated that only the Schirmer tear test showed a significant association with symptoms (Lin, 2005b). However, some studies have refuted these findings and suggested it to have low reproducibility, with wide variations occurring between subjects and on different days/visits and further indicated that the reliability of the test can be affected by environmental conditions, e.g. temperature and humidity. Furthermore, even the position of the eye during the Schirmer test appears to influence the results, with inferior gaze producing a falsely higher result (Bitton, 2013).

2.43 Rose Bengal staining (RB)

Ocular surface evaluation using RB staining is usually done using the RB strips 1% placed for 2 minutes in the lower outer conjunctional cul-de-sac. The stain highlights epithelial surfaces that have been deprived of mucin protein protection having exposed epithelial cell membranes. Mild cases of DES are detected more easily using RB than fluorescein stain and conjunctiva is stained more intensely than the cornea (Tanaka, 1996). RB and Lissamine green stain dead, devitalized cells as well as healthy cells with inadequate protection (Foulks, 1999). The Oxford grading scheme can be used for grading ocular surface damage (Schiffman et al., 2000). The grading chart is made up of five panels, each of which represents typical gradations of stain on either cornea or conjunctiva. Grading is done as 0, I, II, III, IV and V depending on number of dots per panel. Minimum being grade 0 and maximum score is V (Bron, 2003). RB is an important tool in evaluating dry eye, but it is best used as an adjunct due to its lack of sensitivity and specificity (Schiffman, 2000). In one study, the RB test had a high sensitivity of 75.8% but a low specificity of 10.14% (Aditya, 2013). However, a study done in Valladolid, Spain, to calculate internal validity of two DES screening questionnaires and correlate the results with DES diagnostic tests, the test which exhibited the best match was the combination of fluorescein stain and RB (83.2% match).

It is worth noting that RB staining can occur in asymptomatic patients and there is no clearly defined relationship between ocular surface damage specific to dry eye diagnosis and a patient's symptoms (Khan-Lim, 2004). RB has also been reported to be toxic to the corneal epithelium causing stinging sensation upon instillation without anesthesia (Kim, 1999).

2.44 Tear break-up time (TBUT)

TBUT was first introduced by Norn (Norn, 1969) and remains the most frequently used diagnostic test to determine tear film instability (Smith, 2008). Currently, the technique involves instilling sodium fluorescein into the tear film using a moistened strip or a pipette and observing the tear film with a biomicroscope, and cobalt blue light (Cho, 1995). The patient avoids blinking and TBUT is the time interval between a complete blink and the appearance of the first break, discontinuity or dry spot observed in the tear film following a blink. The tear break-up time (TBUT) measures stability of the tear film. The patient has dry eye if a dry spot appears before 10 seconds. The TBUT can be used to evaluate an unstable tear film, leaving the physician to investigate further the cause of the instability and look for surface irregularities or lid margin disease. A study done in India found the sensitivity of Tear Film Break Up Time to be 68.85% and specificity to be 78.32% and found Tear Film Breakup Time to have better chances of diagnosing dry eye than any other tests (Aditya, 2013). Another study done by Mengehar LS and associates showed TBUT to have a sensitivity of (83%) and high specificity of (85%). And according to Goto et al (2002) based on a sample of 80 eyes of 48 healthy subjects, the sensitivity and specificity of TBUT measurements were 75% and 60% respectively, for categorization of dry eye symptoms. Inasmuch as this test is cheap, easy to perform, and uses readily available supplies, its reproducibility and accuracy have been questioned (Vanley, 1977, Lin, 2005b), however, various measures have been taken to improve its diagnostic capability, for example by taking the average score of two or more separate measurements (Nichols, 2004a).

2.5 Diagnosis of DES

DES has continued to present clinicians with a diagnostic dilemma, mainly due to its multiple causative factors and in part due to the complex nature of the disease. Currently, there is no single test or set of tests considered a “gold standard” for its diagnosis and monitoring allowing treatment to be withheld until a patient is symptomatic (Potvin, 2015). Furthermore, although a variety of diagnostic tests are in common clinical usage, there is no consensus on which combination of tests should be used to define the disease, either in the clinic or for the purposes of a research protocol (DEWS, 2007b). The poor correlation between the symptoms that patients present with and the clinical signs that might be observed makes the situation worse since dry eye is basically a symptomatic disease (Yuxin, 2016). At the present time, symptom

questionnaires are among the most repeatable of the commonly used diagnostic tests (DEWS, 2007b) though various tests can be employed to distinguish the different types; the Schirmer test and Tear Break-Up Time (TBUT) are the most commonly used (Merck Manual, 2014**).** However, a study found out that the test which exhibited the best match was the combination of fluorescein stain and Rose Bengal (83.2% match) and therefore advised that the Schirmer test-TBUT diagnostic combination should not be utilized for validating DES (Fuentes-Páez, 2011). Javadi et al (2011) refuted this and suggested that a diagnostic criteria that would include symptoms of the disease, suggestive findings on Schirmer Test (< 5 mm wetting after 5 minutes) and fluorescein and Rose Bengal staining (> 3+) would be considered, however it is difficult to come up with a diagnostic criteria because most diagnostic tests for dry eye disease aren't reproducible, and many emerging technologies are not widely used. To further complicate the issue, there is a large discrepancy between a patient's symptoms and observed signs and even these symptoms may overlap with other diseases (Hyon et al., 2014). It is generally agreed though that tear break-up time (TBUT) of less than 10 seconds and a tear meniscus height of 0.2 ± 0.09 mm or less is considered pathological (EM, 2015b).

2.6 Grading severity of DES

There is still no gold-standard model for determining dry eye severity (DEWS, 2007c, Sullivan et al., 2010). In 2006, a Delphi panel of DED specialists came to a consensus that disease severity is one of the critical factors when considering therapeutic options for DES (Behrens, 2006). They subsequently recommended a DES severity grading which was later adopted by the DEWS (DEWS, 2007a). They categorized severity into four levels, based on increasing frequency and intensity of various signs and symptoms. Patient-reported symptoms included requirement of tear substitute, ocular discomfort and visual disturbance. Clinical signs included conjunctival injection, conjunctival and corneal staining, corneal/tear signs (i.e. filamentary keratitis), lid/meibomian glands, tear break-up time (TBUT; fluorescein based), and Schirmer score.

CHAPTER THREE: METHODOLOGY

3.1 Study Design:

This was across-sectional hospital-based study.

3.2 Setting:

The study was carried out in REC which is a church based fee-paying tertiary eye hospital that has been in existence since the 1960s. The hospital is located in Mbarara Municipality, South-western Uganda approximately four hours' drive from the capital Kampala. The hospital receives approximately 25,000 patients per year mainly from south-western Uganda, parts of north western Tanzania, Rwanda and eastern Democratic Republic of Congo and has a bed capacity of about 100 patients. Services provided include; general outpatients consultation, surgery, and low vision. REC is also currently the only referral center in the entire country for retinoblastoma.

3.3 Study Period:

Data collection periodlasted for a total of 4 months of non-consecutive days from September to December 2017 and the weather condition was generally dry. .

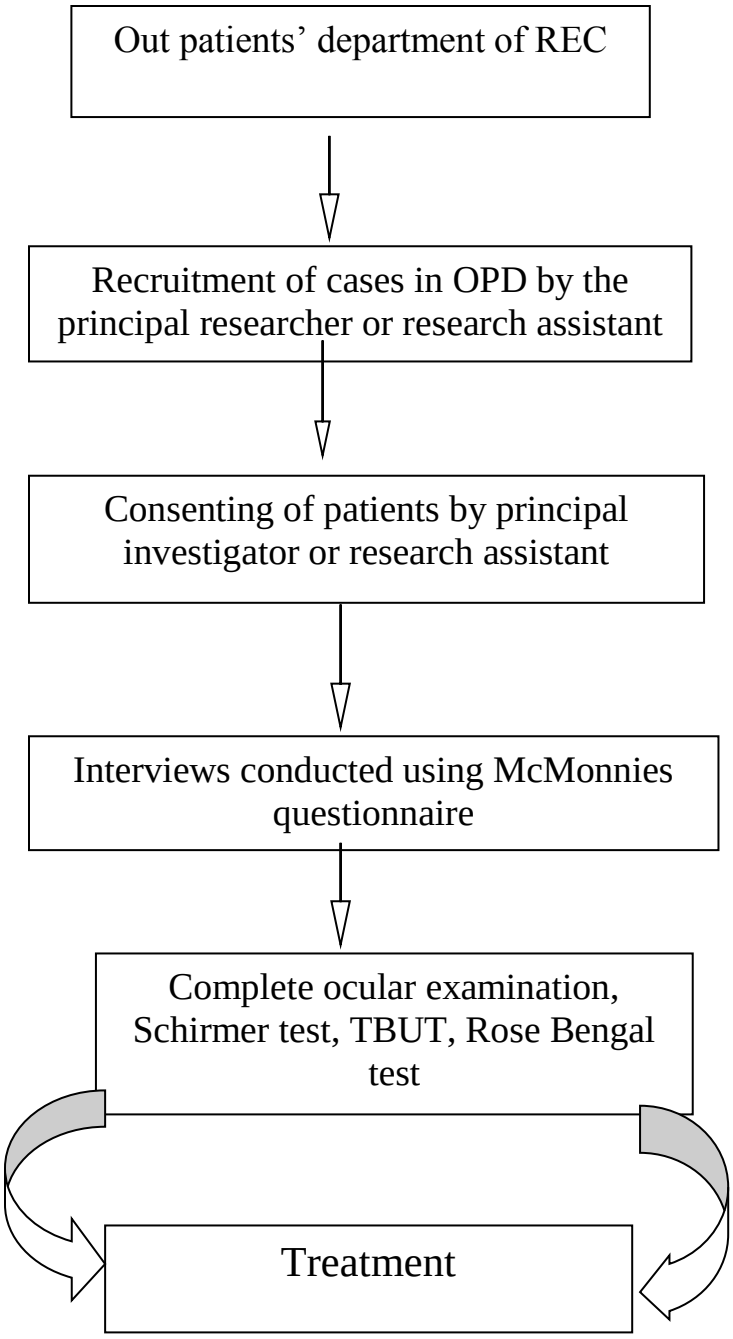
3.4 Study Population:

Included all adults (40 years and above) attending Ruharo Eye Centerduring the study period.

3.5 Sampling Process:

A convenient sampling technique was employed.Basing on the records from the out patient's department, about 20 patients who are 40 years and above attended the clinic daily; and since each patient examination took approximately 30 minutes, a minimum of 10 patients wasrecruited on each of the non-consecutivedays of data collection. The receptionist helped to identify the patients who were 40 years and above who met the inclusion criteria and informed the researcherwho thentook each patient to the examination room from where informed consentwas obtained, MQ administeredand eye examinations performed.

Figure 2: Recruitment of participants (flowchart)



3.6 Study variables

We collected data on the following:Social demographic characteristics such as age, sex, level of education, residence, occupation,McMonnies total score, Schirmer I test results, TBUT test results, and

Rose Bengal test results.The main outcome measure was presence or absence of DES.

3.70 Eligibility criteria

3.71 Inclusion Criteria:

All patients aged 40 years and abovewho consented to the study were recruited.

3.72 Exclusion Criteria:

1. Patients with symptoms requiring acute eye care.
2. Patients who had undergone eye surgery in the past 3 months.
3. Those who refused to consent.

3.8 Sample Size Calculation:

Sample size was determined using Buderer's formula(Buderer, 1996).Since the test was required to be more sensitive than specific, thesensitivity formula wasused to determine the sample size. Therefore using the formula below, the anticipated sensitivity SN = 0.98, absolute precision = 0.03 with 95% confidence level (two-tailed), expected prevalence of DES = 0.18 from an Indian hospital based study(Sahai, 2005).

Sample size (n) based on sensitivity $= \frac{Z^2 1-\alpha/2 \times SN \times (1-SN).}{L^2 \times \text{Prevalence}}$

Sample size (n) based on specificity $= \frac{Z^2 1-\alpha/2 \times SP \times (1-SP).}{L^2 \times (1- \text{Prevalence})}$

Where:

N = required sample size

SN = Anticipated specificity = 97%

SP= Anticipated sensitivity = 98%

α = Size of the critical region, (1- α is the Confidence level), = 0.05

$Z^2 1-\alpha/2$ = Standard normal deviate corresponding to the specified size of the critical region

(α) = 1.96

L = Absolute precision desired on either side (half-width of the confidence interval) of the specificity or sensitivity= 0.05

This gave a total sample size of 167 patients who were 40 years and above.

3.9 Data collection procedure:

Procedure

During the data collection period, a consecutive number of patients who were 40 years and above wereidentified by the receptionist and approached daily in the waiting room of the Outpatients Department (OPD) of REC. The purpose of the study was explained to participants who were then requested to give a written informed consent to participate in the study.

History

Demographic details including, age, sex, address, level of education and occupation were recorded in a data collection tool designed by the principle investigator.

All patients were screened for dry eye using MQ with scores ranging from 0-40. Dry eye screening was done based on these symptoms as follows: normal (<10), marginal (10-20) and pathological dry eye (>20) as per guidelines of MQ. The maximum possible score was 40. Those who scored below 10 were considered as not having DES.All patients were subjected to clinical examination and clinical dry eye tests.

Clinical examination

Patient examination followed the order below:

Visual acuity assessment using Snellen E- chart was done.

The Schirmer 1 test (without anesthesia) was performed by placing the filter stripswhich were 5x35 mm (exported by Devine Meditech) in the inferior temporal fornix with the eye partially closed. The test results was considered positive if the length of wetting obtained was≤ 10 mm in 5minutes.

Slit lamp examination of anterior segment was done to see thepresence of conjunctival hyperemia, and mucus filament, thickening of the lid margin, telangiectasia, and meibomian gland dysfunction which was done by performing gland expression with digital pressure to the central lower lid.

TBUT test was recorded after fluorescein staining using fluorescein strips 1 mg/ml staining (manufactured by Ophtechnics limited)which were wetted using normal saline.The patients were asked to blink several times and then look straight at a target; the time taken for the first dry spot to appear was recorded, and an average of three readings was taken as TBUT. The test was considered positive if average TBUT was ≤ 10s.

Ocular surface evaluation was done using the commercially available Rose Bengal strips1.5 mg/ml staining (exported by Devine Meditech)placed for 2min in the lower outer conjunctional cul-de-sac after wetting using normal saline. The stain highlightsepithelial surfaces that have been deprived of mucin protein protection having exposed epithelial cell membranes. The Oxford grading scheme was used for grading ocular surfacedamage(Schiffman, 2000). The grading chart is made up of five panels, each of which represents typical gradations of stain on either cornea or conjunctiva. Grading is done as 0, I, II, III, IV andV depending on number of dots per panel. Minimum being grade 0 and maximum score is V(Bron, 2003).

Grading of conjunctival hyperemia was done using standard photographs that were printed out to help the principle investigator to make appropriate comparisons.

In all the clinical tests, the more severely affected eye was considered for analysis.

4.0 Data management:

The data set was entered into Microsoft Excel and exported into STATA version 13.0 for analysis. Tabulation of demographic characteristics was done and the percentage of each variable was reported.The prevalence of DES among patients aged 40 years and above presenting at REC was expressed as a proportion of patients diagnosed with DES out of all the patients enrolled in

the study, and the respective confidence intervals were provided. Gender specific DES prevalence was provided in a stratified analysis.

Sensitivity was calculated as the proportion of true cases (people with DES) correctly categorized as having the disease by the instrument, and specificity as the proportion of true non-cases (healthy people) correctly categorized as being healthy. Since no single test is considered a "gold standard", a composite score was formed using Schirmer I test and TBUT to act as the gold standard. A score of "one" was assigned to a positive test and a score of "zero" to a negative test and summation of the scores were taken as the composite score.A composite score of one and above was taken as DES, for example, if the TBUT and Schirmer I scoreswere zero and one respectively, the result would be interpreted as positive; if both scored one, the result would still be positive but negative if both scores were "zero"

In determining the sensitivity and specificity of the questionnaire in grading severity of DES, Schirmer, TBUT and Rose Bengal tests were used.The patients' findings were designated as normal, mild/moderate or severe for each individual measure. Since there was no consensus in literature indicating appropriate threshold for distinguishing between mild and moderate values, all patients with disease severity grades greater than normal were combined into a single mild/moderate group.

The severity designations used for grading Schirmer I were as follows: greater than 10 mm, normal; 5-10 mm, mild/moderate; and 0-4, severe.

The severity designations used for grading TBUT were as follows: greater than 10 seconds, normal; 5-10 seconds, mild/moderate; and 0-4; severe.

The severity designations used for grading Rose Bengal were as follows: 0-1, normal; 2-3, mild/ moderate; 4-5, severe.

A value of 1 was assigned to a normal grade for each measure, 2 for a mild/moderate grade, and3 for severe.

The values for the three measures were then summed up to generate a final severity score: less than or equal to 3, normal; 4-7, mild/moderate; and 8-9, severe.

For example, if a patient's test results were normal, mild/moderate and normal respectively, scores of 1 point, 2 points and 1 point would be assigned then the summation of these points (1+2+1=4) would be interpreted asmild/moderate DES because the sum falls in the range between (4-7)(Sullivan et al., 2010).

	Schirmer	**TBUT**	**Rose Bengal**	**Summation (composite)**	**Diagnosis**
Patient 1	1	2	1	4	Mild/moderate DES
Patient 2	1	1	1	3	Normal
Patient 3	2	3	3	8	Severe DES

4.1 Quality Control:

The questionnaire was verified and piloted on 10 participants who were not included in the study. No changes were made to the questionnaire after the pilot study.

The questionnaire was also translated into Runyankole so that non- English speaking patients would understand the questions.

The questionnaire was filled by the patient with the help of an assistant to ensure that participants understood each question.

Data was double checked by the principal researcher before entering them into Microsoft Excel to identify any duplication and missing information.

For patients who had already participated in the study, their files were marked to avoid the risk of picking on them in the subsequent sessions.

4.2 Ethical consideration:

Approvals were sought from the department of Ophthalmology, Faculty Research Committee and Institutional Ethical Review Committee of Mbarara University of Scienceand Technology (Number: 07/07-17) and REC. Informed consent was obtained from all the participants. The participants were given opportunity to ask questions regarding the study. No information was withheld from the patient about the findings of the ocular examination. Participant's data

weresecurely kept during the course of the study in a password protected computer. Participants were informed that participation in the study is voluntary and that refusal to participate would not affect their management and they would still be entitled to their routine care. Participants were also informed that their names would not be used in any way during the study. Numbers were used to identify their data.

4.3 Limitations

Data collection was done during a generally dry period which might have influenced the proportion of DES since DES is exacerbated by dry weather conditions.

We were not able to collect data on consecutive days because of the tight academic schedule.

4.4 Dissemination of results:

The final report will be submitted as a dissertation to the Faculty of Medicine as part of the requirement for the Master of Medicine in Ophthalmology. Copies of the document will be given to REC, MUST library, and Office of the Dean, Faculty of Medicine. The results of the study will be presented to the department of Ophthalmology, REC,COECSA and MUST annual scientific conference. The manuscript will also be submitted in peer review journals for publication by JOECSA. Community awareness on DES will be incorporated during outreach activities.

CHAPTER FOUR:RESULTS

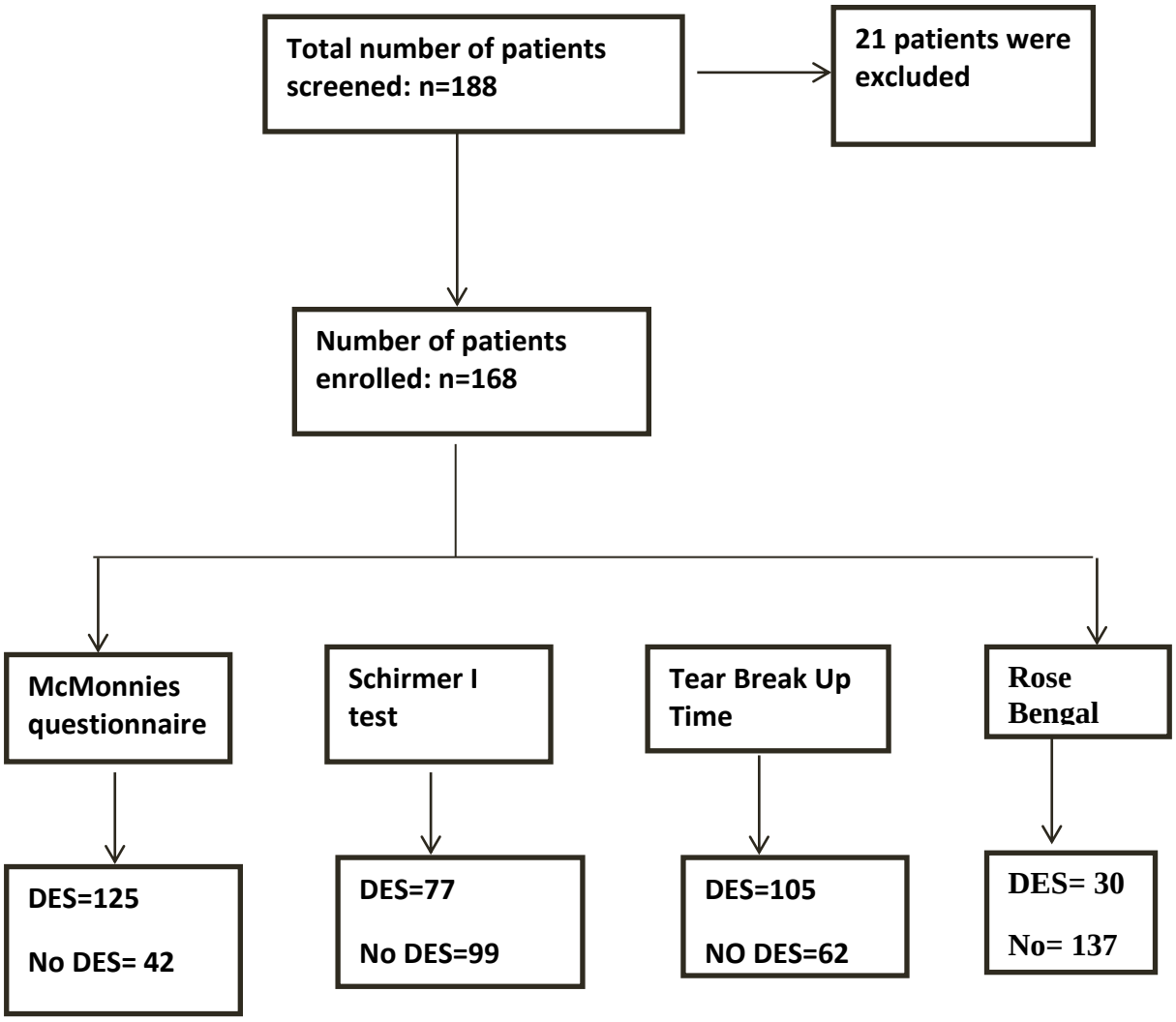
4.1Introduction

In this chapter, we aim to describe the study profile of patients who were enrolled in this study as well as presenting the results: validity of McMonnies questionnaire in diagnosing and grading severity of Dry Eye Syndrome among patients who are 40 years and above attending REC using composite scores derived from summation of the various clinical tests.

4.2 Study profile

During the study periodwhich lasted 34 non consecutive days from 25th Septemberto 15th December 2017, a total of 2,108 patients attended REC and of these, 938 were 40 years and above. Of the 938 patients,188 patients were screened for DES by convenient sampling method. A total of21 patients were excluded (15 underwent cataract surgery, 3 had acute anterior uveitis and the remainder had bacterial conjunctivitis) as a result of not fulfilling the eligibility criteria; therefore 167patients were included in the study analysis.

Figure 3: Study profile



4.3 Base line characteristics

Out of the 167 patients enrolled, 91 (54.49%) were females. The female to male ratio was 1.2:1. The median age of the patients was 63 years(IQR 54-72 range 40-94).Most of the patients underwent some form of education111 (66.47)while 56 (33.35%) had no formal education. The majority, 124 (74.25) were peasants.The median Schirmer I score was 14mm (IQR 5-22range of 1-35), while that of TBUT score was 6.67 seconds (IQR 3.33-17, range of 1-34.33) and that of MQ was 12 (IQR 9-17 range of 2-27).

Table 1:BASELINE CHARACTERISTICS N=167

Variable	**Description**	**Frequency**	**%age**
Age	40-50	30	17.96
	51-60	44	26.35
	61-70	47	28.14
	>70	46	27.54
Sex	Male	76	45.51
	Female	91	54.59
Occupation	Peasant	124	74.25
	Unemployed	10	5.99
	Professional	17	10.18
	Business	11	6.59
	Casual Labourer	5	2.99

Education Level	No Formal Education	56	33.53
	Primary	79	47.31
	Secondary	18	10.78
	Tertiary	14	8.38

Table 2: CLINICAL EXAMINATION FINDINGS N=167

Variable	**Description**	**Frequency**	**%age**
Eyelids	Normal	164	98.20
	Retracted	0	0
	Ectropion	1	0.60
	Entropion	2	1.20
	Lagophthalmos	0	0
Eyelid Margin	Normal	160	95.81
	Erythema	1	0.60
	Abnormal deposits	1	0.60
	Keratinized	5	2.99
Meibomian gland orifices	Plugged	11	6.59
	Open	156	93.41
Eye lashes	Normal	164	98.20
	Trichiasis	3	1.80
	Distichiasis	0	0
Conjunctiva Hyperemia	Absent	92	55.09
	Mild	57	34.13
	Moderate	18	10.78

	Severe	0	0
Pannus	Yes No	165 2	98.8 1.20
Mucus filament	Present Absent	35 132	20.96 79.04

4.4 Proportion of patients with dry eye syndrome

The proportion of patients with DES was 68% as determined by the composite score.The proportion of females and males who had DES was 70% and 66% respectively with a P value of0.530. The proportions of DES based on the individual tests are shown in the table below.

Table 3: PROPORTION OF PATIENTS WITH DES AS DETERMINED BY MQ AND THE DIFFERENT CLINICAL TESTS

Test	**Frequency**	**Proportion**
Composite score	114/167	68%
Schirmer I	65/167	46.1%
TBUT	105/167	62.9%
Rose Bengal	30/167	18%
McMonnies Questionnaire	125/167	74.9%

Table 4: McNEMAR'S TEST FOR STATISTICALLY SIGNIFICANT DIFFERENCE BETWEEN SCHIRMER AND TBUT

The test provides a strong evidence to reject the null hypothesis of no difference between the two tests.

TBUT			
Schirmer	**DES**	**NO DES**	**Total**
DES	**11 a**	**66 b**	**77**
NO DES	**51 c**	**39 d**	**90**
Total	**62**	**105**	**167**

$X^2=(b-c/b+c)^2$

$X^2= (66-51/66+51)^2$

$X^2= 0.02$

Table 5: McNEMAR'S TEST FOR STATISTICALLY SIGNIFICANT DIFFERENCE BETWEEN MQ AND COMPOSITE SCORE

The test provides a strong evidence to reject the null hypothesis of no difference between the two tests.

Composite score			
MQ	**DES**	**NO DES**	**Total**
DES	**93 a**	**32 b**	**125**
NO DES	**21 c**	**21 d**	**42**
Total	**114**	**53**	**167**

$X^2= (b-c/b+c)^2$

$X^2= (32-21/32+21)^2$

$X^2= 0.04$

4.5 Sensitivity and specificity of McMonnies questionnaire in diagnosing DES

The sensitivity and specificity of McMonnies questionnaire in diagnosing DES were 81.6% (95% CI,73.2 - 88.2) and 39.6% (95% CI,26.5 - 54) respectively. A positive predictive value of 73.4% and a negative predictive value of 50% were found as shown below.

Table 6: CALCULATION OF VALIDITY INDICES

Composite score			
MQ	**Positive**	**Negative**	**Total**
Positive	**93 a**	**32 b**	**125**
Negative	**21 c**	**21 d**	**42**
Total	**114**	**53**	**167**

Sensitivity=a/a+c

Specificity=d/b+d

Positive predictive value=a/a+b

Negative predictive value=d/c+d

Table 7: SENSITIVITY AND SPECIFICITY OF MCMONNIES QUESTIONNAIRE IN DIAGNOSING DES

Validity indices	**Score**	**95% CI**
Sensitivity	81.6%	73.2%-88.2%
Specificity	39.6%	26.5%-54%
PPV	73.4%	65.8%-81.8%
NPV	50%	34.2%-65.8%
Likelihood ratio (+)	1.35	1.07-1.71
Likelihood ratio (-)	0.465	0.279-0.774

4.61 Grading of DES

According to the grading of the composite score (Schirmer I, TBUT and Rose Bengal),the biggest proportion of patients,111 (66.47%) had mild/moderate DES, 54 (32.34%) were normal while the rest had severe DES as shown below.

Table 8: GRADING OF DRY EYE USING A COMPOSITE SCORE OF SCHIRMER I, TBUT AND ROSE BENGAL

Grade	**Frequency**	**Percentage**
Normal	54	32.34
Mild/moderate	111	66.47
Severe	2	1.19

McMonnies questionnaire graded the majority of patients, 104 (62.28%) as having mild/moderate DES, while Schirmer, TBUT and Rose Bengal tests graded most of the patients as normal as shown below.

Table 8: GRADING OF DES USING MQ, SCHIRMER, TBUT AND ROSE BENGAL TESTS n=167

Test	Normal (%age)	Mild/Moderate (%age)	Severe (%age)
MQ	42 (25.15)	104 (62.28)	21 (12.57)
Schirmer	102 (61.08)	52 (31.14)	13 (7.78)
TBUT	68 (40.72)	66 (39.52)	33 (19.76)
Rose Bengal	137 (82.03)	28 (16.77)	02 (1.20)

The sensitivity and specificity of McMonnies questionnaire in grading the severity of DES were 61.1% and 18.6% for normal; 63.6% and 40.4% for mild/moderate and 50% and87.9% for severeas shown below.

Table 9: SENSITIVITY AND SPECIFICITY OF MCMONNIES QUESTIONNAIRE IN GRADING SEVERITY OF DES

MQ	Normal (95 % CI)	Mild/Moderate(95% CI)	Severe (95% CI)
Sensitivity	61.1% (46.9-74.1)	**63.6%** (53.9 - 72.6)	**50%** (1.26 - 98.7)
Specificity	18.6% (11.9-27)	**40.4%** (27.6 - 54.2)	**87.9%** (81.9 - 92.4)
PPV	26.4% (18.9-35)	**67.3%** (57.4 - 76.2)	**4.76%** (0.12 - 23.8)
NPV	50% (34.2-65.8)	**36.5%** (24.7 - 49.6)	**99.3%** (96.2 - 100)
LR (+)	0.75 (0.51-0.92)	**1.07** (0.826 – 1.38)	**4.13** (0.972 – 17.5)
LR (-)	2.09 (1.26-3.49)	**0.901** (0.604 – 1.35)	**0.569** (0.142 – 2.28)

There was a statistically significant relationship between McMonnies scores and the Schirmer and TBUT tests in as far as grading is concerned but that of Rose Bengal staining showed no significant relationship as shown in the tables below.

Table 10: COMPARISON BETWEEN MCMONNIES SCORES AND TBUT GRADING OF DES n=167

McMonnies Questionnaire	**TBUT**				
	Normal	**Mild/moderate**	**Severe**	**Total**	**P-value**
Normal (<10)	20 (47.62%)	19 (45.24%)	3 (7.14%)	42	
Mild/moderate(10-20)	45 (43.27%)	39 (37.50%)	20 (19.23%)	104	
Severe (>20)	3 (14.29%)	8 (38.10%)	10 (47.61%)	21	**0.003**
Total	68	66	33	167	

Table 11: COMPARISON BETWEEN MCMONNIES SCORE AND SCHIRMER I GRADING OF DES N=167

McMonnies Questionnaire	**Schirmer**				
	Normal	**Mild/moderate**	**Severe**	**Total**	**P-value**
Normal (<10)	42 (100%)	0	0	42	
Mild/moderate(10-20)	60 (57.69%)	44 (42.31%)	0	104	
Severe (>20)	0	8 (38.10%)	13 (61.90%)	21	**<0.001**
Total	102	52	13	167	

Table 12: COMPARISON BETWEEN MCMONNIES SCORE AND ROSE BENGAL GRADING OF DES n=167

McMonnies Questionnaire	**Rose Bengal**				
	Normal	**Mild/moderate**	**Severe**	**Total**	**P-value**
Normal (<10)	38 (90.48%)	4 (9.52%)	0	42	
Mild/moderate(10-20)	86 (82.71%)	17 (16.35%)	1 (0.96%)	104	
Severe (>20)	13 (61.90%)	7 (33.33%)	1 (4.76%)	21	**0.062**
Total	137	28	02	167	

CHAPTER FIVE: DISCUSSION

McMonnies Questionnaire (MQ) is among one of the earliest and most widely used screening instruments for dry eye syndromes (Nichols et al, 2004b). It is still also the only patient perspective instrument specific for Dry Eye disease that has a formalized grading scheme and some published psychometric properties (McMonnies, 1987a, McMonnies, 1987b). The aim of this study was to assess the Validity of MQ as a screening and grading tool for DES among patients aged 40 years and above attending Ruharo Eye Centre (REC), South western Uganda and these were our key findings.

5.1 Proportion of patients with DES

The proportion of patients with DES was high, with more females reportedlyhaving DES as compared to males but this finding was not significant as shown in other studies(McCarty CA, 1998, Aditya, 2013, Lee, 2002) possibly because of our small sample size(McCarty CA, 1998).But in overall, the proportion of patients with DES in this populationwas much higher than the results obtained from an Indian-based hospital study which reported an overall DES prevalence of 18.4% andon stratification by age group, a prevalence of 58.4% was reported among those who were 40 years and abovewhich was still lower than what we obtained(Sahai, 2005) and for the overall prevalence of27.5 %, and 37.6% in the 40-49 year old age group obtained in a population based study in Indonesia(Lee, 2002).

The high prevalence in our setting may be partly explained by the fact that our study utilized a composite score of Schirmer and TBUT that would obviously beexpected to capture more cases of DES than would be the case if each was scored alone, as proven by a significant McNemar's test that we carried out. However, we might have probably overestimated this proportion considering the fact that our data collection took place in the dry season, nevertheless, this result still confirmed how common DES is amongst this population, a finding quite in agreement with many other studieseven if their prevalence values were not as high as that obtained in our study(Liu, 2014, Moss et al., 2000).

The 75% (125) proportion of DES as determined by McMonnies index alone was far much higher than that shown by either Schirmer or TBUT alone (46.1% and 62.9% respectively), a finding which could be perhapsattributed to its poor correlation with other clinical test results as

reported by some studies(Hay, 1998, Schein, 1999, Nichols, 2004b) or probably it could highlighting it as a better screening tool for DES.

5.2 Sensitivity and specificity of McMonnies questionnaire in diagnosing DES

McMonnies questionnaire (MQ)is still the only patient perspective instrument specific for Dry Eye disease that has a formalized grading scheme and some published psychometric properties (McMonnies, 1987a, McMonnies, 1987b). We used a composite score because no clinical test is considered gold standard for diagnosing DES and in particular, we chose these two tests because they proved to be highly sensitive and specific in most studies (Schiffman, 2000, Bjerrum, 1996, Farris, 1983, Versura, 2007, Bartlett, 2011). Our study found the sensitivity of MQ to be good. This finding was similar to that reported by Nichols et al.(Nichols, 2004b) who found a sensitivity and specificity of 82% and 36% respectively using a composite score of Schirmer I and TBUT and Yuxin et al.(Yuxin, 2016) who found an overall sensitivity and specificity of 80.3 and 49.7 respectively with a cut off of 12.5 for McMonnies questionnaire.

All of these studies employed the modified scoring system developed by Nichols as was the case in our study but none of them was of an African cohort. It's worth noting that previous studies using this questionnaire revealedvarying values of sensitivity (34%–98%) and specificity (36%–97%); possible reasons for these variations may include the difference in the experimental population (McMonnies, 1987b, McMonnies, 1998, Nichols, 2002, Nichols, 2004b). McMonnies et al(McMonnies, 1998) studied a group of 50 women with Sjögren syndrome who had severe DES while our study included all patients who were 40 years and above, irrespective of their diagnosis and our study population was of African descent.

Furthermore, different scoring methods of the MQ have been used since its development. In our study, we adopted the modified scoring system developed by Nichols and associates (2004b) which could possibly explain why the two findings were similar in contrast to the weighted algorithm based on clinical experience used by McMonnies et al.(McMonnies, 1998) whose sensitivity and specificity estimates were higher(92% and 93% respectively) but one cannot rule out the possibility ofselection bias sincethey assessed efficacy based on the data from the same sample of patients from whom the cutoff values for diagnosis were derived and not from an independent sample of new patients.

We thought of looking at age and gender stratifications of sensitivity and specificity by MQ but we did not feel that these comparisons would be necessarily fair because the scoring algorithm for the McMonnies Index automatically weights women higher than men, and older individuals higher than younger individuals

5.3 Sensitivity and specificity ofMcMonnies questionnaire in grading DES severity

Our sensitivities and specificities were quite low, but not surprising since MQ was originally not designed as a grading tool. Gothwal and associates (Gothwal, 2010) actuallyquestioned the role of MQ as a measure of disease severity (McMonnies, 2010), nevertheless, they suggested that it would most likely function well as a grading tool in a different population with a greater spread of disease severity. Based on this conclusion, we believe that our study would have probably yielded better sensitivities and specificities if not for the fact that we had a narrow spread of disease severity and asmaller sample size.

To the best of our knowledge, only a few studies (Moore, 2009, Nichols, 2004b, Yeo, 2003)have been published on the sensitivity and specificity of MQ in grading DES but none of these used the index score for grading therefore adequate comparisons were nearly impossible. Nichols et al. and associatesreported a fair performance of MQ in differentiating mild-moderate from severe DES and poor accuracy in predicting patients with severe disease (Nichols, 2004b).

One other study on the other hand, (Bhatnagar KR, 2015)seems to say otherwise. In their study, they usedMcMonnies score to divide people into normal (MI<10), moderate (MI 10-20) and severe dry eye (MI>20) groups, and found positivecorrelations between MQ score and clinical test results. Therefore we are quite convinced that McMonnies score can reflect disease severity to some degree.

Among those with severe symptoms (MS>20), 85.7% had a low TBUT (<10s), 100% had a low Schirmer I test (<10 mm) implying that the findings of the questionnaire are quite similar to that of the clinical tests as shown by the overall statistical significance of association (p= 0.003 and <0.001) respectively. Our findings were similar to that of Lin and associates (Lin, 2005a) and Bhatnager and associates (Bhatnagar KR, 2015) who found associations between symptoms and clinical tests but differed from the study conducted by Nichols (Nichols, 2004b) who found poor relation between dry eye tests (TBUT and Schirmer) and symptoms except for rose Bengal staining which showed some slight discrepancies, forexample, in the subgroups of patients with

severe DES (MQ scores >20) , 33.33% of patients were rated as having mild/moderate DES (grade 2-3).

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

1. The proportion of patients with DES in this population was high (68%).
2. The severity of DES in this population was predominantly mild/moderate.
3. The sensitivity of the MQ in diagnosing DES was good.
4. The specificity of MQ in diagnosing DES was low.
5 The sensitivity and specificity of MQ in grading DES was also low.

6.2 Recommendations

1. Based on the high proportion of patients with DES in this study, we recommend routine screening of all patients who are 40 years and above for DES.
2. Based on the good sensitivity of MQ in diagnosing DES derived from thisstudy, the use of MQas a screening tool for DES is highly recommended in order to help identify the cases that will require further clinical assessment for DES.
3. Since the specificity of MQ in diagnosing DES was low, patients diagnosed with the tool as not having DES require further clinical assessment especially when they have symptoms suggestive of DES.
4. Based on the low sensitivity and specificity of MQ in grading the severity of DES, we do not recommend its use for this purpose.Further studies should be done with a bigger sample size so that conclusive observations can be made regarding the sensitivity and specificity of the questionnaire in grading DES in this setting.

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