THE PREVALENCE OF DRY EYE AMONG ADULTS WITH INFLAMMATORY EYELID, CONJUNCTIVAL AND CORNEAL DISEASES AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA

A Cross sectional descriptive study at Muhimbili eye clinic

BY

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CERTIFICATION

The undersigned certify that he has read and hereby recommend for acceptance by the University of Dar es salaam a dissertation entitled: The prevalence of dry eye among adults with inflammatory eyelid, conjunctival and corneal diseases at Muhimbili National Hospital in partial fulfilment of the requirements for the degree of Master of Medicine (Ophthalmology).

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DECLARATION

AND

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I, Dr Anna Sanyiwa declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or other degree award.

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DEDICATION

To my lovely husband and my son Austin.

To my late beloved father mzee John Sanyiwa, who died during the course of this work.

To all my teachers, who made it possible for me in this profession.

ABSTRACT

Objectives: This study was designed to determine the prevalence of dry eye among adult patients with eyelid, conjunctival and corneal inflammatory diseases attending outpatient eye clinic at Muhimbili National Hospital.

Methods: For a period of one year (February 2000 to January 2001) a total of 200 consecutive new patients, who presented with one or more symptoms of dry eye often or all the time were seen at Muhimbili eye clinic. The patients underwent a comprehensive detailed history and examination. A standardized clinical slit lamp examination was performed on all patients included in the study. Four objective assessments of dry eye were made: tear film break up time, Schirmer test, rose bengal staining and fluorescein corneal staining. Dry eye was diagnosed if a symptomatic patient had abnormality of one or more of the clinical tests. A positive clinical test was defined as: Schirmer ≤ 5mm, tear break up ≤10 seconds, rose be ngal score >3 and fluorescein score >3.

Results: The population examined varied in age from 20-82 years with a mean age of 37.8 years. Females comprised 69.5% and males 30.5%. Dry eye was diagnosed as follows: 20% by tear break up time, 7% by Schirmer test, 9% by rose bengal stain and 7% by fluorescein stain. Of the study population 2.5% had normal tear stability with low tear secretion, 4.5% had both low tear secretion and stability and

15.5% had normal tear secretion with low tear stability. Tear secretion and tear stability decreased with increasing age ($p<0.0001$ and 0.04) respectively. Females comprised the majority of patients with low tear secretion. There was a statistically significant correlation between tear secretion and tear stability ($p<0.00001$). Among the study group 16(8%) had visual impairment. No patient was blind. The visual impairment was more among patients with low tear secretion and low tear stability. Sand like sensation, soreness, blurred vision and morning eye pain were the symptoms felt most in patients with low tear stability or low tear secretion. Symptoms experienced by patients with normal tear secretion or tear stability were itching, soreness, tearing and sandy like sensation.

Conclusion: The present findings suggest that dry eye is prevalent among patients with eyelid, conjunctival and corneal inflam matory diseases in Dar es salaam. A combination of symptoms and clinical tests is needed for the diagnosis of dry eye syndrome. The prevalence of dry eye varied depending on the test used to diagnose the condition.

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INTRODUCTION AND LITERATURE REVIEW

Dry eye is one of the major eye problems necessitating frequent visits to the ophthalmologists.[1,2] Dry eye is a very common disorder affecting a significant percentage of the population, particularly those older than 40 years, all over of the world. Its prevalence is not well documented, but it is thought to increase with increasing years.[3,4,]

Dry eye occurs when tear film lacks sufficient quality or quantity to maintain a healthy cornea and conjunctiva.[5,6] Dry eye is now defined as "a disorder of the tear film due to tear deficiency or excessive evaporation that causes damage to the interpalpebral ocular surface and is associated with symptoms of discomfort."[7] There are several different potential causes of dry eye. The most common cause is an insufficient acqueous layer of the tear film. A deficiency in the outer lipid layer causes excessive evaporation, leading to dry eye. Other factors contributing to poor quality of tear are eyelid globe defects, blinking mechanism dysfunction and mucin deficiency.[2,5,6] The patients with dry eyes of different causes usually have similar complaints. The symptoms include chronic unremitting painful eye, irritation described as sandy gritty sensation that usually becomes worse as the day goes on, blurred vision, photophobia and redness. Other symptoms are a feeling of dryness and sometimes reflex

tearing. Certain activities may be related to a worsening of symptoms, such as reading, using a computer and concentrating on a fixed task. These activities result in a decreased blink rate. A work environment in which there is low humidity, increased air currents, exposure to air conditioning, smoke, and makeup applied excessively to the eyelids can be associated with a tear film abnormality and dry eye.[2,6,8,9]

Dry eye is a chronic condition that requires regular attention. In its milder form it is a discomfort rather than a danger to vision. Severe dry eye however causes damage to corneal epithelial cells and may compromise the cornea and predispose it to secondary infection, which can lead to irreversible sight threatening conditions.[2,5,6,9]

The clinical tests used to diagnose the disease are said to be not accurate whereas the laboratory tests are very accurate. However there are no reasons whatsoever to discard the present clinical tests. For example finding Schirmer test 1 consistently lower than 5mm in 5 minutes is an easy way to strongly suspect a dry eye state.[10,11]

Most clinicians still rely on traditional diagnostic tests, such as tear breakup time, the Schirmer test and ocular surface dye staining, for diagnosis of dry eye disease. It is now recognized that a diagnostic approach that uses many diagnostic tests is better than that which uses a single test in identifying a patient's dry eye state.[12]

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Prevalence and incidence: -

There are no clear data on the epidemiology of dry eye worldwide. The prevalence and incidence in the general population has not been determined. Various studies have reported different prevalence rates.[3,4,13,14,15,16,17]

In a very recent large-scale Beaver Dam eye study, whereby the cohort was aged 48-91 years, the overall prevalence was 14.4%. Prevalence varied from 8.4% in subjects younger than 60 years to 19% in those older than 80 years. Age adjusted prevalence in men was 11.4% compared with 16.7% in women. The risk factors found to be associated with dry eye were smoking, use of caffeine and multivitamin.[14]

Similarly a recent cross sectional prevalence study in Melbourne, Australia used several methods of diagnosing dry eye i.e. an interviewer-administered questionnaire, the Schirmer test, tear break-up time, fluorescein and rose bengal staining of the cornea and conjunctiva. Dry eye was diagnosed if one or more of the tests had abnormal value. The study yielded an overall dry eye diagnosis as follows: 10.8 % by rose bengal, 16.3% by Schirmer test (cut off point<8mm), 8.6% by tear break up time, 1.5% by fluorescein staining, 7.4% with two or more signs, and 5.5% with any severe symptom. The paper reported a number of cases that were diagnosed based on severe symptoms but without the presence of any sign.[4]

A population-based prevalence study, which was done, to study the demographics and estimate the prevalence of dry eye among elderly Americans was performed in residents of Salisbury, Maryland. The patients were aged 65 year and older. After completing a standardized questionnaire pertaining to dry eye symptoms, the subjects underwent Schirmer and rose bengal tests and anatomic assessment of meibomian glands. In this population, 14.6% were symptomatic, defined as reporting one or more dry eye symptoms often or all the time, 2.2% were symptomatic and had a low Schirmer test results, and 2% were symptomatic and had a high rose bengal test score. Furthermore, 3.5% were symptomatic and had either a low Schirmer score or a high rose bengal score, and 0.7% were symptomatic and had both a low Schirmer score and high rose bengal score. No association of symptoms or signs were seen with age, sex, or race. The study concluded that symptoms and signs of dry eye are common among the elderly. Extrapolating to the United States population aged 65 to 84 years, the study yields an estimate of 4.3 million who experience symptoms of ocular irritation often or all the time.[3]

Another survey was done in Japan to ascertain the prevalence of dry eye in consecutive new outpatients seen in eight Japanese centres. All underwent comprehensive examination, including double vital staining and measurement of tear break-up time. They discovered

that 17% of consecutive new out patient had dry eye and they came up with the conclusion that dry eye is one of the most common ocular disorder encountered by physicians. [15]

A study with questionnaire approach was done in Canada where by a 13-point questionnaire was mailed to all optometric practices in Canada. A total of 28.7% of recruited patients reported dry eye symptoms, 24.2% reported concurrent dry mouth, 24.5% had worse symptoms in the morning, 30.3% reported concurrent lid problems and 35.7% reported a history of allergies. The prevalence of reporting any level of symptoms of dry eyes was approximately 1 in 4. Severe symptoms were reported by 1 in 225 patients.[16]

The frequency of keratoconjuctivitis sicca in person s aged 30-60years in Copenhagen is estimated to be 11% according to the Copenhagen criteria and 8% according to the preliminary European criteria.[16]Dry eye was studied in Pakistan where the age range of the patients was from under 20 to over 60 years .The visual acuity at the time they reported was 6/60 or less in 70% of patients and 6/18 or above in 30%. 50% of patients were hopelessly blind and 20% were with very poor prognosis. Only 30% patients had a chance to escape impending blindness.[17]

In India consecutive cases of dry eye were studied to comment upon its epidemiological aspects. The incidence of dry eye was 0.46%.[18] In each of these studies, the criteria used to diagnose dry eye varied.[3,4,13,14,15,15,16,17,18]

Tear film structure and composition

The tear film is approximately 7-10micromols in thickness. It is composed of three discrete layers, first described by Wolf, the lipid, acqueos, and mucin layer from anterior to posterior.[19]

The Lipid layer

The lipid layer was originally postulated by Wolf and subsequently described, via interface pattern, by McDonald.[19] In1972, Brauninger and coworkers[20] demonstrated directly the presence of a superficial lipid layer. The lipid layer is approximately 0.1 thick, it is secreted primarily by the meibomian glands. (30-40) in the upper lid and (20-30) smaller gland in the lower lid.[21] A small portion may also be produced by the sebaceous gland of Zeis located in the palpebral margin of the tarsus and Moll gland, which is located at the root of each eyelash.[8,21] The functions of the lipid layer is to inhibit evaporation of the tears, especially under condition of low humidity and turbulent air flow[22]. It also protects the aqueous layer from polar lipid contamination that would tend to rupture the tear film prematurely.[22] Furthermore, the lipid present at the meibomian gland orifices acts as a hydrophobic barrier to prevent the overflow of the tears.[23] As the lipid spreads over the aqueous layer, it drags along with it additional fluid, thus slightly thickening the tear film. The removal of the lipid layer increases the rate of evaporation four fold.[9]

The aqueous layer

The bulk of the tear film consists of the aqueous layer, which is about 7micromiters thick. It is composed of 98% water and 1.8% solids, numerous solutes, electrolytes, proteins, enzymes, urea, amino acids and glucose. The aqueous layer accounts for over 90% of the thickness of the tear film. It is reported that 95% of aqueous tear arise from the orbital and palpebral portion of the main lacrimal gland. The rest of the tears are produced by the glands of Krause and Wolfring, distributed along the upper and lower cul-de-sac.[21]

Tears also contain certain enzymes which are known to have antimicrobial properties i.e. lysozyme an important tear antimicrobial constituent which is also a useful diagnostic parameter in evaluating tear dysfunction.[24] Lysozyme an antibacterial substance described first by Fleming in 1922 [25] is responsible for the low bacterial count of normal human tears. It has been assumed that the lacrimal gland is able to synthesize the enzyme.[26] Other enzymes with antibacterial properties include beta-lysin and lactoferin. The primary source of lactoferin is the main and accessory lacrimal glands. Lactoferin plays a role in the antimicrobial defence of the external eye. Lactoferin has also a role in the complement system.[8,21] Lactoferin concentration in tears is a useful indicator of the main and accessory glands function. Interferon is also present in tears. It inhibits viral replication and is efficacious in limiting the severity of ulcerative herpetic keratitis.[8, 21]

A number of enzymes involved in glucose and amino acid metabolism are present in tears. Collagenase secreted by corneal epithelium, keratocytes and polymorphonuclear leucocytes degrades stromal collagen. Antiproteases are also found in the tear i.e., aplha1-antitypsin and alpha2-microglobulin.[21] Other enzymes present in tears are hydrolases, such as acid and alkaline phosphatase which are associated with break down of tissue.[21]Tears have the nine complements component required for the classic and alternate complement fixation pathways. There are also anticomplement factors, which interact with complement factors and play a role in modulating inflammatory disease and antimicrobial defence of the external eye.[9,21] Immunoglobulins found in tear include IgA, IgM, IgE, IgG and IgD. IgA is formed by plasma cells in the interstitial tissues of the main accessory lacrimal gland and subtantia propria of the conjunctiva. IgA plays a role in local host defence mechanism of the external eye. Individuals manifesting vernal conjunctivitis demonstrate elevated tear and serum levels of IgE.[27] Increased levels of tear histamine support the concept of conjunctival mast cell degranulation triggered by IgE-antigen.[2,9]

Electrolytes and small molecules regulate the osmotic flow of fluid between the corneal epithelial cells and tear film .The principal ions of the tear film are Na, K, Cl and bicarbonate. The Na concentration of tear parallel that of serum while concentration of K is 5-7 times

greater than in the serum .Na, K, Cl regulate the osmotic flow of fluid from the cornea to the tear film. Bicarbonate regulates tear pH. Other tear electrolytes (Fe, Cu, Ca, PO) are enzymes cofactors.[20] The protein concentration in the tear is low being of the order of 0.1-0.6 % by comparison with 6-7% for plasma.

The Mucin layer

The surface of the corneal epithelium is hydrophobic. Mucin is extremely hydrophilic. The mucin layer is 0.02 to 0.05micromiters thick. This innermost mucin layer of the tear film coats the microplicae of the cornea superficial epithelial cells and forms a fine network over the conjunctival surface. The mucin creates a hydrophilic layer, which is essential for the even and spontaneous distribution of the tear film.[21] It also interacts with the tear lipid layer to lower surface tension, thereby stabilizing the tear film. The loose mucous network covering the bulbar conjunctiva traps exfoliated surface cells, foreign body particles and bacteria. Mucus has another important function in the eye, that of maintaining the stability of tear film.[2,9] Tear mucins are secreted principally by the conjunctival goblet cells and minimally by lacrimal gland cells. The goblet cells are located throughout the palpebral and fornix conjunctiva, but are concentrated in the inferior nasal area. The average goblet-cell count in the normal human eye is 8.8 glands per mm square. [28]

Functions of tear film

The tear film performs several important functions in the eye

1.Forms and maintains a smooth refracting surface over the cornea, since the greatest change in refraction of light occurs at the interface between air and precorneal tear film. Corneal surface is not a perfectly smooth surface and so the tear film serves to fill in irregularities in the corneal epithelium, producing a smooth initial refractive surface.

2.Maintains a moist environment for the epithelial cell of the cornea and conjunctiva. Preventing the outer layer of the eye from drying is fundamental to normal eye function. Should the tear fail to do so, the resulting dry spots can generate not only gritty or burning sensation, but also epithelial cell damage and potentially the loss of sight.

3.Has bacterialcidal properties as it contains several enzymes like interferon, lysozyme, Beta -lysin and immnologlobulins. In this way it minimizes the possibility of eye infection.

4.Lubricates the lids and ocular surface during blinking. Without proper lubrication, friction can lead to abrasive damage, with similar result as that due to ocular drying.

5.Transports metabolic products (primarily oxygen and carbon dioxide) to and from the cornea.

6.Nutrition: The nutrients in the tear film directly nourish the cornea.

7. The tear film is also important in removing foreign bodies and it dilutes, and washes away noxious stimuli.

8.It acts as an access route for white blood cells from the perilimbal blood vessels which, help in the healing of central corneal wounds.[4,6,9]

Pathophysiology of dry eye

Understanding of the pathophysiology of the disease is crucial in interpreting and evaluating diagnostic tests. The tests for dry eye are useful in that they lend some degree of objectivity to what is essentially clinical diagnosis. Dry eye is an ocular surface disease that results from decreased tear secretion and or increased tear film evaporation. Evidences recorded over recent years have proposed that the decreased tear secretion or increased tear film evaporation or both result in elevated tear film osmolarity which is the final common pathway for numerous disorders that can cause dry eye. It is now evident that increased tear osmolarity is the link between changes in the lacrimal glands, lids, and the diseases of ocular surface. The most convincing data comes from studies of pre-clinical model of lacrimal gland disease and meibomian gland dysfunction. In these studies the ocular surface changes of dry eye disease have been shown to be consistent with, dependent upon and proportional to increase in tear film osmolarity.[29,30,31]

It is now know that dry eye disease evolves cumulatively over long time through a sequence of four (4) milestones:

1.Decreased tear production or increased tear evaporation with an increase in tear osmolarity.

2.Decreased conjunctival goblet cells density.

3.Increased corneal epithelial desquamation.

4.Destabilization of corneal tear interface [32,33,34,35,]

Clinical features

The symptoms of dry eye include dryness, gritty sandy like sensation, which is persistent and painful. Burning sensation in the eyes when in areas of low humidity or pollution. Patient may complain of excessive tearing, possibly due to reflex secretion. Foreign body sensation frequently associated with punctate keratopathy, photophobia, blurred vision, eye tiredness[36], irritation, soreness[37], and redness are the other possible complaints. In the early stages of the disease, the symptoms it causes may seem to come and go, but the symptoms become more persistent as eye dryness worsens. Most patients experience greater discomfort as the day progress. Patients with blepharitis, the discomfort tends to be greater in the morning but lessens during the day.[2,5,69,21]

The signs of dry eye include conjunctival vascular dilatation, conjunctival pleating and a decrease in tear meniscus. Irregular

corneal surface, increased debries in tear film, superficial punctate keratitis, sterile corneal ulceration (which is a serious complication of keratoconjunctivitis sicca) [38] corneal erosion and corneal filaments. The corneal lesions are best demonstrated by the instillation of rose bengal stain or fluorescein dye. [2,9]

Causes of the dry eye

The causes of dry eye are varied and include congenital disorders, aging, systemic diseases, neuroparalytic defects, trauma, irradiation, and drugs. These causes of dry eye can be grouped into disorders of the three layers of the tear film and lid or corneal surface. [2,9] Lipid abnormality occurs in patients with blepharitis and meibomianitis.[39] These are the most common cause of evaporative dry eye states.[39] Studies done in United States and Japan have demonstrated that this is a very common clinical condition involving about 60% of patients with ocular irritation.[40,41] Frequently, the meibomian glands are occluded and infected so that abnormal direction of the lashes develop.[2,9] In these patients the tear film is compromised.[39] Increased evaporation of the tear film is also caused by increased exposure of the globe, such as seen with thyroid eye disease. In Graves disease the eyeball is pushed out of the socket, exposing more of the eye surface. Increased exposure leads to increased evaporation rate.[42] Other causes are over correction of ptosis, ectropion and

lagopthalmos. Disorders that do cause mucin layer deficiency are vitamin A deficiency, pemphigoid, Steven-Johnson syndrome and chemical burn as a result of conjunctival disease and loss of goblet cells.[2,6,9] Acqueous deficiency occurs in congenital diseases like Riley-Day syndrome or familial dysautonimia.[2,6,8] Females comprise the vast majority of the aqueous deficiency patients. The trouble appears to begin during menopause when estrogen and androgen levels decline. It appears that androgen help prevent leukocytic infiltration of the lacrimal gland by stimulating the glandular cells to produce antinflammatory cytokines.[8] When androgen levels decline, T cells apparently activate the lacrimal gland, produce factors that inhibit secretion and promote an inflammatory process.[42,43,44] This ends in gland dysfunction and aqueous deficiency. In both aqueous deficiency and meibomian gland diseases, patients develop reduced corneal sensitivity. This creates a vicious cycle. The stimuli for basal secretion are no longer present, so the ocular surface becomes dry. The epithelium becomes inflammed and ultimately becomes metaplastic and unable to produce mucin, the tear film layer that stabilizes the aqueous and lipid layers.[7,10,45] Many patients appear to have perfectly normal tear films but complain of dry eye symptoms, especially those with mebomian gland diseases.[7,10] In these patients the tear clearance is reduced. The tears are not normally washed away and remain on the ocular surface for an excessively long time,

especially in the night.[42] Hence irritating symptoms are worse upon awakening in the morning.[41] Slow tear clearance is a problem because the tears accumulate inflammatory mediators and free radicals, which lead to ocular surface inflammation.[7] This causes patients to experience classic dry eye symptoms and yet exhibit none or few of the signs.[1,42,41]

Several factors can contribute to dry eyes and some of them are discussed.

Age: Advancing age is the single most important risk factor for dry eye, as the lacrimal gland output decreases with age although dry eye can occur at any age. It is estimated that nearly 75% of people over the age of 65 years will experience dry eye.[39]. Age also is associated with decline in corneal sensation and meibomian gland dysfunction.[2,9,42]

Sex: Dry eye occurs in both men and women although most common in women. Hormonal changes brought on by pregnancy, lactation, oral contraceptives, menstruation and menopause [46,47] can cause dry eye condition. About 3 million Americans have dry eye as a result of Sjogren's syndrome, and 90% of these patients are women.[49]

Trachoma: It is a chronic keratoconjunctivitis caused by *Chlamydia trachomatis.*[9] Clinical diagnosis can be made on the presence of two or more signs. The signs include lymphoid follicles on the upper tarsal plates, typical conjunctival scarring, vascular pannus, limbal

follicles or their sequelae, the Herbets pits.[50] Disabling sequelae are trichiasis, entropion and corneal scarring. Pathologically trachoma represents a primary involvement of the conjunctival and corneal epithelial cells followed by secondary chronic inflammatory changes in subepithelial tissues. Necrosis of subepithelial tissue and tarsus is followed by cicatrisation and deformation of ocular tissues. The conjunctiva becomes stratified squamous epithelium, goblet cells are lost with resulting deficiency of mucous, and ductules of the lacrimal gland may be occluded with subsequent tear deficiency and development of keratitis sicca. [2,9]

Xerophalmia: A term used to describe ocular surface changes due to of vitamin A deficiency. The conjunctival changes characteristic of vitamin A deficiency are usually confined to bulbar region. Features include dryness, Bitots spots, lack of wettability, loss of transparency, thickening, wrinkling and pigmentation.[8,9] In corneal xerosis the cornea is rough, lusterless, keratinized, stromal oedema and superficial punctate keratitis visible with biomicroscope. There is lack of wettability of the cornea even in the presence of an apparent normal tear supply. The tear film break up time is much decreased as the result of decreased goblet cell density.[8,9 51]

Stevens- Johnson syndrome: The postinfammatory mucosal scarring that occurs as result of severe erytherma maltforme, where conjunctival mucous membranes are involved can result in chronic

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dry eye. Resolution of the acute mucosal necrosis leaves subepithelial fibrosis, which causes symblepharon. Scarring of the accessory lacrimal glands and the ducts of the main lacrimal gland cause tear film deficiency. The combination of trichiasis, incomplete blinking, keratinization of the lid margin and reduced tears are features in the involved eye. Frequently bacterial and non-bacterial inflammations, superficial punctate erosion with eventual neovascularization, cornea ulcer and varying degree of reduction of vision accompany this condition. [39,49]

Human Immunodeficiency Virus (HIV): Dry eye is one of the ophthalmological finding in HIV infection. It can occur before the beginning of the Aids stage.[52] The main problem is decreased tear production. It has been reported that dry eye occurs as a single entity in approximately10- 20% of male testing positive for HIV infection, typically at later stages of the illness.[52] The prevalence of dry eye among females was found to be higher than males in another study which found the prevalence to be 20 –25%.[53] The increased frequency was not related to the severity of HIV disease.[53] The possibility of autoimmune like pathogenesis of abnormalities of tear production in patients with HIV infection is not clear. If encephalopathy is also present, incomplete lid closure, a decreased blink rate or both may exacerbate the condition.[54]

Sjogrens syndrome: It is a chronic autoimmune disorder with multsystem abnormalities. The disease is characterized by mononuclear infiltration of the lacrimal and salivary gland, leading to destruction of the ductules and acina structure and resulting in deficiency of tear and saliva. Sjogrens may occur alone but is often associated with other autoimmune diseases. Sjogrens syndrome has insidious onset and usually occurs in middle age. Over 90% of patients are females. Patients with Sjogrens syndrome have keratoconjunctivitis sicca from deficiency of aqueous tear secretion of the lacrimal glands. The Schirmer test is usually less than 5mm and the tear breakup time may be reduced.[2,9,39]

Herpes zoster ophthalmicus keratitis: Characteristically there is course punctate epithelial keratitis, which later goes on to develop nummular type of stromal opacity. Other characteristic signs are dendritic ulcer with some similarities to those seen with severe herpes simplex keratitis and decreased cornea sensation. A mild to moderate reduction in tear volume is sometimes observed in these patients. In addition the tears appear to wet the cornea poorly in some eyes. Drying can be so extreme that as in the fifth nerve lesions, single or multiple dellen can be seen.[9,39]

Chemical burns: As sequelae of chemical burns, there is loss of the accessory lacrimal glands or scarring of the ductules and opening of the major lacrimal gland, which may result in tear deficiency. The

tear film may be unstable as a result of mucin deficiency state produced as a result of a diffuse loss of goblet cells.[2,5,6, 9]

Cicatrial pemphigoid: It is a chronic, cicatrizing conjunctivitis.[56] The disease affects women more than men (2:1). It is usually seen in patients over the age of 60 years and is rarely seen before the age of 30 years.[55] Patients frequently present with recurrent attacks of mild nonspecific conjunctival inflammation with an occasional mucopurulent discharge. Recurrent inflammation of conjunctiva can lead to destruction of goblet cells and eventually mucin deficiency. Scarring of main and accessory lacrimal gland ductules may occur resulting in aqueous tear deficiency. [2,6,39]

Clinical diagnosis of dry eye : The diagnosis of the tear film abnormality or dry eye is made by clinical judgment after consideration of the history, clinical examination, laboratory tests, and, in some cases, the results of a therapeutic trial.[7] A patient's history and chief complaint can immediately alert the clinician to the possibility of a dry eye. Drugs that the patient may be using, such as antihistamines, vasoconstrictors, antihypertensives, and anticholinergics can be associated with decreased tearing.[2,6,9]

The clinical examination for a possible dry eye is performed in such a way that stimulation of reflex tearing is avoided.

Tear meniscus: Tear meniscus is the clinical test commonly done to evaluate patients with dry eye. Assessment of the tear film meniscus is quantitative, minimally invasive, and is a direct measurement of tear film quantity.[55] The tear meniscus reportedly contains 75-90% of the tear volume[56] and studies using semi quantitative methods found that tear meniscus reduction corresponded to the decreased volume in tear-deficient dry eyes.[57,58] Tear meniscus parameters, such as tear meniscus height (TMH) and radius of the tear meniscus curvature (TMR), have been shown to be sensitive indicator in evaluating tear-deficient dry eye.[55] Also there are reports that tear volume can be regarded as abnormal if TMH is <0.10mm.[59,60] It is a useful test, when used in conjunction with the other existing tests for dry eye. The inferior marginal strip is examined before taking visual acuity. Using the magnification of the slit lamp with only room illumination, the fluorescein stained tear meniscus height is observed.[9]

Tear break up time (BUT); was originally described by Norn [61] in 1969. He described it as cornea wetting time. The concept of BUT was popularized by Lemp and Hamil in1973. [62] Its measurement depends on the fact that given enough time the tear film will thin and eventually rupture (even in normal eyes). Break up time is a measure

of the length of time the eye can be kept open before the tear film ruptures spontaneously. It is the only measure of the relative instability of the tear film, and the abnormal results could have many causes. It is defined as the time interval between a complete blink and initial development of a random dry spot on the corneal surface.[9] Tear break up time of less than 10 seconds is considered indicative of unstable tear film and 10-15 seconds is considered borderline.[10,24]

The test is performed by placing a drop or a paper strip of fluorescein in the lower conjunctival cul-de-sac, asking the patient to blink several times, and then scanning the stained tear film with the cobalt blue light. The lids must not be touched nor elevated above their normal open position. The end point is recorded in seconds at the first appearance of a dry spot. A dry spot appears as a black area on the corneal surface where there is no wetting (no fluorescein), surrounded by the normal fluorescein-marked tear film. It is important to remember that any elevation on the corneal surface will cause almost instantaneous breakup of the tear film. For this reason, dry spots must occur at random locations to be counted as accurate end points. The test should be repeated several times and an average taken.[2,9,63]

Several points are important when performing the test. First, the examiner must not touch the patient's eyelid. This manoeuvre tends to extend the interpalpebral fissure and thus artificially shortens the

BUT. Secondly, the areas of break up time must appear in a random pattern to be counted as tear film break up. The reason for this is to avoid counting areas of epithelial irregularity or elevation, which will thin the tear film and cause rapid break up time. Thirdly, the solution in which the fluorescein is dissolved may theoretically play a role on BUT measurements. Some academics suggest that the preservatives in ophthalmic irrigation solution and even fluorescein paper strip itself may artificially lower the BUT. Some of these preservatives have detergent action and may break up the superficial lipid layer of the tear film causing it to rupture prematurely.[62,63,64,65] It is better to use a non-preserved type of fluorescein such as fluoresoft.[64] It is also not advised to use drops, as these will increase the volume of tear film. Another potential problem in clinical BUT evaluation is that the smoothness, or lack therefore, of the corneal epithelium has a great influence on tear film stability. In many of the diseases associated with tear abnormalities there are underlying epithelial irregularities, which make is hard to interpret the BUT measurement. About half of dry eye patients will have normal film stability.[61] However the BUT test has a great deal of potential as a useful clinical measurement. It is non-invasive and a measurement of the common denominator of tear film abnormalities in these cases where there is loss of tear film stability.[2,9,39]

Schirmer's test I: Schirmer was the first person to describe Schirmer test.[9] Schirmer test1 is generally used in a clinical setting, inspite of its notorious variability. The Schirmer test remains the most commonly performed clinical test for dry eye. Other tests are basically laboratory and research oriented.[10,24] Over the past years the minimum acceptable wetting values has dropped. Most reasonable is the suggestion of Van Bijsterveld, [10,24] who found that using a cut-off value of 5.5 mm of wetting in 5 minutes, the correct diagnosis could be made in 83% of dry eye patients tested. In most parts of the world, the Schirmer test is still the main test used by optometrists for the assessment of tear adequacy in screening for potential contact lens wearers and as an aid in the diagnosis of dry eye. It can be used with added confidence if repeated measurements give consistently low readings.[2,9,10,24]

The purpose of this test is to measure the total (reflex and basal) tear secretion.[9] To minimize reflex tearing, the eyes should not be manipulated before starting this test. There are no contraindications to this test. The materials used are the commercially available Whatman No. 41 filter paper strips 5 mm wide x 30 mm in length, known as Schirmer tear filter strips. The patient is seated in a dimly lit room, and the filter paper strips are folded 5 mm from the end. The folded end is placed gently over the lower palpebral conjunctiva at its lateral one-third. The patient keeps the eyes open and looks upward.

Blinking is permissible. After 5 minutes the strips are removed and the amount of wetting is measured from the folded end. If the strips are completely wetted before 5 minutes, they may be removed prematurely. A normal patient will wet from 10 -30 mm in 5 minutes. This is age dependent and decreases after the age of 60 years but is rarely less than 10 mm in 5 minutes. Measurements greater than 30 mm at 5 minutes indicate that reflex tearing is intact but not controlled and, therefore, are of little diagnostic value. Between 10 and 30 mm of tear secretion may be normal, or basal secretion may be low but compensated for by reflex secretion. Values less than 5 mm on repeated testing indicate hyposecretion of basic tearing. There is a 15% chance of diagnostic error in this test.[2,5,6]

Some variations in Schirmer testing exist and merit some comment. For years, people have argued over whether the Schirmer test should be done with or without topical anaesthesia. Those who do Schirmer test without anaesthesia, argue that this is actually more physiological. On the other hand, those who use anaesthesia argue that without it one is not measuring physiologic tear flow parameters but merely the patient response to discomfort.[65] Some general facts are known about the mean responses of population to the Schirmer test done with and without anaesthesia. When a large group of normal subjects was tested without anaesthesia, the mean wetting value was 20mm.[9] When the same volunteers were tested with

anaesthesia, the mean value was 12mm.[9] Thus it can be concluded that topical anaesthesia tends to decrease Schirmer values by about 40 percent when mean values of large population are compared.[65] Unfortunately, wide individual variation exists, and so this decrease is not realized in every single patient.[9]

Rose Bengal stain: The clinical use of rose bengal has been greatly promoted since 1933, when Sjogren [9] described a unique staining pattern in patients with keratoconjunctivitis sicca syndrome. Without direct evidence, Sjogrens and later Passmore and King[67] speculated that rose bengal stained desquamated epithelial cells. It was not until Norn's [68,69,70] work was published between 1962 and 1970 that the foundation was laid for the current concept that rose bengal stained only degenerated or dead cells and mucus strands. Based on this concept, 1% rose bengal has been used clinically to establish the diagnosis of keratoconjunctivitis sicca.[71,72,73,74] and to interpret other lesions such as epithelial dendrites of herpes simplex or zoster, dysplastic or squamous metaplastic cells of conjunctival squamous neoplasms, and various forms of superficial punctate keratitis. Rose bengal, a red aniline dye, is a derivative of fluorescein but is different from fluorescein in several important ways.[39] Rose bengal does not stain the precorneal tear film, as does fluorescein. Instead, it seems to precipitate at the bottom of the meniscus. Unlike fluorescein, rose bengal is able to stain cell nuclei and cell cytoplasm. On the other

hand, fluorescein is able to permeate through a disrupted epithelial layer and diffuse among the intercellular spaces. Rose bengal also stains mucus and filament, whereas fluorescein stains only mucus. [9] [49] Rose bengal 1% is an extremely valuable test in the diagnosis of sicca and deserves to be used more extensively. It has only one disadvantage, irritation upon instillation. The irritation seems to be directly related to the amount of epithelial damage present on the corneal surface and, to some extent, the size of the drop. It is frequently possible to alleviate some of the pain by dropping the rose bengal onto a wooden end of cotton tip applicator and then touching the eye with the applicator. When using rose bengal to evaluate dry eye it is helpful to divide the palpebral aperture of each eye into three zones (medial, central corneal, lateral) and record the amount of staining in each eye according to van Bijsterveld scores. In the van Bijsterverd scoring method, 1 point refers to the staining of single points, 2 points refers to scattered pattern, and 3 points to staining of confluent areas of the ocular surface. In this way, each eye could receive a maximum score of 9, if stained maximally in all three zones. A score of 3 or more for one eye is considered abnormal.[10] [24] Rose bengal score is strongly related to the damage of superficial epithelium of the cornea and conjunctiva in patents with dry eye. Two false positives can be seen with rose bengal stain i.e., small amount of staining over the body of a pterygium or pinguencula is a common

normal finding. [5,9] If Schirmer test has been performed before the use of rose bengal stain, the conjunctiva will pick up the dye in an area of contact between the conjunctiva and the paper strip. Anything that can damage the epithelium like infection, trauma and toxic reactions can cause rose bengal staining. These are spurious findings and not indicative of abnormal tearing. It is characteristic of dry eye to produce a pathognomonic pattern. This pathognomonic pattern consists of two triangles of stain on the conjunctiva within the palpebral fissure, with their bases on the limbus.[9]In severe cases, a connecting band across the cornea is always seen. This area corresponds to the exposed surface of the eye within the palpebral fissure. The rose bengal dye test yields direct evaluation of epithelial cell damage and indirect measurement of tear volume deficiency. Rose bengal also stains mucus, which is often a prominent finding in dry eye conditions. [2,6,9]

Rose bengal can be applied into the ocular surface in two ways .One involves wetting the tip of a commercially available rose bengal strip with sterile saline, followed by brief application of the strip to the conjunctival surface. A 1% rose bengal solution may also be used and applied to the ocular surface in drop form. The liquid rose bengal seems to yield better results than rose bengal strip but may be more irritating on instillation. This is probably related to the concentration of the dye reaching the eye.[9,24,66]

Fluorescein stain: Historically Pfluger[73] was the first to use fluorescein to stain rabbit corneal epithelia abrasions. Later Straub,[74] Fromm and Groenouw[75] introduced it for clinical use to detect various corneal epithelial lesions, using a non-fluorescence light microscope. The conventional interpretation of fluorescein staining has been based on the concept that fluorescein perfuses readily in tissue fluid and between cells. Up to the present, fluorescein delivered as 0.25% solution or via a paper strip has clinically been applied to detect corneal epithelial abrasion in various forms of punctate keratitis or epithelial defects and to examine the status of precorneal tear film with respect to break up and contact lens fitting. Also to evaluate tear volume and clearance, to detect aqueous humour flow, leakage and to measure corneal epithelial and endothelial permeability.[2,9,39]

Fluorescein is a resorcinol opthalein, the water-soluble sodium salt. It is used for vital staining. It produces diffuse greenish yellow staining of the preocular tear film and the lacrimal river along the lid margin, which is best visible in the cobalt filtered light. This staining facilitates a proper judgment of the tear film and the tear film break up (BUT).[65] Fluorescein penetrates thorough defects of the cornea and conjunctiva epithelium into the intracellular fluid, thus staining the defect and surrounding zone. It gradually diffuses between epithelial cells through Bowman's membrane into the corneal stroma.

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and the endothelium and may finally stain the aqueous humor as well. [97-100] -Fluorescein dye will stain corneal or conjunctival surface any time epithelial integrity is compromised. Although fluorescein staining is relatively nonspecific, occurring with any condition affecting epithelial integrity, characteristic staining pattern can be helpful in diagnosis of dry eye syndrome. For example in acqueous deficient patients, staining is interparpebral and may be prominent along the inferior.[58] corneal and conjunctival surface. In someone with exposure keratitis secondary to nocturnal lagophthalmos or Bells palsy, staining may occur exclusively in the inferior corneal and conjunctival surface. The fluorescein staining of the cornea is investigated by a scoring method. The cornea is divided into five parts. One to three points are given. 1 point refers to the staining of single points; 2 points, scattered pattern and 3 points, staining of confluent areas within each of the five sections. Staining points of each division are summed to 15 maximum points. In summary a score of more than 3 is regarded abnormal.[10,24,66]

Impression conjunctival cytology: Conjunctival cytology is a simple, non-invasive and cheap method for the study of the ocular surface in dry eyes. It is the most specific and sensitive method, providing valuable information for diagnosis and therapeutic control of dry eye disorders.[10,11] It is a microscopic evaluation of epithelial cell changes characteristic of dry eye disorders on the conjunctiva. In this technique a specimen of one to three cell layer thick is collected by application of circular disc of cellulose acetate filter material in the ocular surface. The characteristic changes seen include decreased goblet cell density, squamous metaplasia of epithelial cells and presence of increased inflammatory cells.[76,77,78,79,80,81,82]

Other tests: Although there has been many attempts to develop additional testing procedures to aid in the evaluation of patients with dry eyes, none has gained wide spread clinical acceptance because of questions regarding their validity as well as practicality in the office setting.[10,11,24] Included are the determination of lysozyme and lactoferin concentrations in the tear film. Both of these proteins are produced by the lacrimal glands and are present in reduced concentrations in dry eye.[5,9] One method used to determine lysozyme concentration is referred to as the agar diffusion lysozyme test. Here, a tear saturated Schirmer strip is placed on an agar medium inoculated with suspension of micrococus lysodeikkticus bacteria. Lysozyme, a bacteriolytic enzyme will then cause a zone of lysis around the strip, which is correlated with lysozyme concentration.[83,84,85,86] Evaluation of lactoferin concentration has been marketed with commercially available assay, called the Lactoplate test (Eagle vision, Inc, Memphesis, TN). With this test, a small disc of tear –wetted filter paper is placed on an agar surface for 72 hours followed by measurement of precipitate ring, which is correlated with lactoferin concentration.[2,9] Lactoplate testing is not sensitive enough to allow accurate diagnosis for the population of mild to moderate dry eye subjects.[87] In summary, measurement of tear lactoferin concentration alone in the basal tears has not shown

to be sufficiently sensitive and specific test for the diagnosis of dry eye than the other clinical tests.

Tear film osmolarity, which has been determined to be higher in-patients with dry eyes, has also been inconsistently used in the evaluation of the dry eye patients. Osmolarity measurement of nanometer tear samples collected from the inferior margin tear strip has been shown to be the most sensitive and specific diagnostic test for dry eye.[88,89] The loss of water from the tear film is accountable for increased tear osmolarity. The usefulness of the tear osmolarity measurement is limited only by the effort required to perform the measurement.[90,91]

Management of dry eye

Although there have been many recent advances in the treatment of dry eyes, the treatment of dry eye does not offer cure but does provide numerous modalities that offer relief of symptoms. The aims of treatment of dry eye are to relieve discomfort, provide a smooth optical surface and prevent structural corneal damage.[57] One approach is to identify the mechanism of tear film dysfunction and then prescribe treatment that corrects or compensates for that defect. The following sequence of therapy is indicated.

Tear replacement. Artificial tears form the main treatment of mild to moderate dry eye. It is crucial that patient uses the drops frequently and regularly. In severe cases the drops have to be instilled at half

hourly or hourly intervals. In milder cases instillation of four times daily may suffice.[9] The main disadvantages of drops are their short duration of action and development of sensitivity to the preservatives. It has been reported that benzalkonium chloride may be toxic to the ocular surface epithelum.[92,93] Essentially there are three types of tear substitutes in the market. These include cellulose derivatives, polyvinly alcohol and mucomimetis.[66] Mucomimetics creates a stable hydrophilic corneal surface and enhance corneal wetting. Mucolytic drops may be useful in patients with corneal filaments and mucous plaques.[5,6]

Bandage contact lens: Soft contact lens, occupy a unique place in the treatment of dry eye. Hydrophilic bandage lenses often provide a tear reservoir but must be used in conjunction with replacement tears.[27] Patients are prone to contact lens intolerance and superinfection and should be followed carefully. Bandage lens is most helpful in three situations: filamentous keratitis, mucin deficiency dry eye with adequate aqueous phase and exposure keratitis. Relief from pain is almost instantaneous, and the filaments seem to melt away under the bandage lens.[39]

Punctal occlusion: Punctal occlusion preserves the natural tears and prolongs the effect of the artificial tears.[2,5,6] Temporary punctual occlusion can be achieved by insertion of 0.2-0.4mm collagen plugs or miniature Teflon plugs. Permanent occlusion of the puncta is

achieved by electrocutery after local anaesthesia.[39] Temporary occlusion may be used to predict those patients who would suffer from epiphora if permanent occlusion were performed. Application of a hot platinum spatula to the punta after local anasthesia provides temporary closure to establish the risk of epiphora.[9 39]

Other methods: Treatment of associated conditions is also important. Interference with the normal lubrication and cleansing function of the tears as well as the association of decreased lysozyme content place the patient at risk for chronic low-grade infections.[39] Such infections of the eyelid margin can aggravate the underlying tear deficiency and should be treated with adequate lid hygiene and antibiotics therapy when necessary.[2,6,9,39] Moist chambers achieved by an occlusive plastic shield across the eye have helped in some cases. Close-fitting glasses with side shield often achieve the same effect. Parotid transplants and mechanized pumps with implanted tubes to the conjunctival sac have been used with limited effectiveness.[39] Consistent with immunologic mechanism for development of dry eye, antinflammatory therapy has been reported to improve both symptoms of irritation and ocular surface disease.[94] Topically applied corticosteroids and a potent immunosuppressive cyclosporin have been reported to improve the irritation and ocular surface signs of dry eye. Lateral tarsorrhaphy can be the last resort to decrease tear evaporation.[1,2,9]

STUDY RATIONALE AND STATEMENT OF THE PROBLEM.

No one knows how many people suffer from dry eye in Tanzania, as no study has been done. This study was done to explore its epidemiology in Dar es salaam. The study was intended to increase our understanding of dry eye disease in-terms of our ability to diagnose as well as treat this traditionally challenging eye disease.

Broad Objective:

To determine the prevalence of dry eyes among adult patients with eye lid, conjunctival and corneal inflammatory disease attending outpatient eye clinic at Muhimbili National Hospital from February 2000 to January 2001.

Specific Objectives:

1. To determine the demographic pattern, blindness and visual impairment among patients with dry eyes.
2. To determine the proportion of patients with dry eyes with normal tear stability and low tear secretion.
3. To determine the proportion of patients with low tear stability but normal tear secretion.
4. To determine the proportion of patients with both low tear stability and tear secretion.
5. To determine the proportion of patients with epithelial defect as demonstrated by positive rose bengal and fluorescein staining.

Methods and Materials:

Study Population: Included in the study were all new consecutive patients aged 20 years and older with inflammatory eyelid, conjunctival and corneal diseases with symptoms and signs of dry eye attending Muhimbili National Hospital out patient eye clinic from February 2000 to January 2001.

Sample size:

Was estimated by using a formula designed for population survey in cross sectional studies as given in EPINF06 package.

$$N = \frac{Z^2 P (1-P)}{D^2}$$

Where Z= 1.96 (Confidence Interval at 95%)

P= 15% - Estimated proportion of subjects with the disease=(0.15)

(1-P) = Expected proportion of subjects without the disease=1-0.15=0.85

D= Marginal error = 0.05, N= Number of subjects required

P= 15% according to the Beaver Dam, Melbourne and Salisbury studies.

$$N = \frac{(1.96)^2 \times 0.15 \times 0.85}{(0.05)^2} = 196$$

From that formula the estimated sample size was about 200 patients.

Study design: This was a cross sectional descriptive study.

Patients selection: Consecutive new patients aged 20 years and above who presented with inflammatory eyelid, conjunctival and corneal disease were recruited and evaluated for symptoms and signs of dry eyes. Tests to evaluate tear film abnormality were carried out to prove whether they had dry eyes or not. These patients were also evaluated for other systemic diseases, which were related to dry eyes. The patients who had symptoms without signs of dry eyes were also included in the study.

The patients at the initial visit were evaluated as follows: Hospital registration number, name of the patient, age, sex, addresses, whether they were from rural or urban areas, and the occupation of the patients were recorded. A detailed history was taken and recorded in the data sheet with particular attention paid to the symptoms of dry eye. Symptoms like, sandy like sensation, transient blurring of vision, burning pain, tearing, dryness, itching and soreness. An informed consent was obtained from the patients. Those patients found to have symptoms of dry eye were further evaluated.

Ocular Examination:

·The best-corrected visual acuity was taken and recorded using Snellen's/ Illiterate E-Chart.

Eyelids:

The eyelid was examined for any defects like coloboma, lid closure abnormality or inflammation (blepharitis).

Slit lamp examination:

By using the slit lamp increased mucus strands and debris were looked for, as these are early signs of dry eye.

The marginal tear meniscus was examined for any abnormality. Tear meniscus height was observed using slit lamp. The tear meniscus was examined after staining with fluorescein. The patient was seated on the slit lamp; the dimmed beam was targeted to the inferior stained tear meniscus. The tear meniscus height was observed from the lower lid margin to the top of the meniscus, with conjuctival or corneal background. The results were recorded as low or absent if the tear meniscus was concave or not seen.

Corneal examination:

The following signs of dry eye on the cornea were looked for:-

- Superficial punctate keratitis, which mainly involved the inferior cornea.
- Corneal filaments consisting of small coma shaped opacities with the unattached end hanging over the corneal surface and which moved with each blink.
- Corneal erosion or epithelial defect were evaluated and recorded.

Clinical Tests:

The following diagnostic tests to evaluate dry eyes were performed:-

Schirmer test without anaesthesia: This test was done to measure the total (basic and reflex) tear secretion. This test was performed before any manipulation of the eyelids, refraction, tonometry or instillation of any eye drops were done, since all of these would stimulate reflex tearing. Commonly used standardized strip of filter paper measuring 35 x 5mm, was used. The strip was folded at the notch 5mm from one end and placed over the lower eyelid margin, at the junction of the lateral and middle third. The test was done simultaneously for both eyes with the patient in a sitting position and the lights dimmed. The patient was instructed to keep both eyes open but blinking normally. Gaze was fixed slightly upwards to help avoid corneal irritation and subsequent reflex tearing. After 5 minutes the strips were gently removed and the extent of wettness on the strips was measured in millimetres from the point at which the strip was folded for placement over the eyelid margin. If the strips were completely wetted before five minutes they were removed prematurely. The value less than 5mm were regarded as abnormal. Values more than 5mm were recorded as normal.

Tear break up time:

This test was done to evaluate the stability of the patient's tear film .A fluorescein strip (fluorets) was put into the lower conjunctival fornix of the eye to be examined. The patient was asked to blink 2-3 times to distribute the dye. The test was performed under the slit lamp by asking the patient to stare straight ahead and not blink, and without touching the patient's eyelids, the examiner scanned the cornea with cobalt blue light of the slit lamp watching for an area of tear film rupture manifested by a black island within a green sea of fluorescein. The tear break up time is the time in seconds between the last blink and the appearance of the dry spot. Break up time of less or equal to 10 seconds was regarded as low tear stability. A break up time of more than 10 seconds was considered to be normal. The dry eyespots, which were considered abnormal, were the ones, which occurred at random locations. The test was repeated three times and an average time was taken. The persistent appearance of dry eyespots in an area was excluded.

Rose bengal stain:

This vital stain was used to evaluate conjunctiva and cornea epithelia. The commercially available 0.5% rose bengal stain was instilled 1-2 drops to the lower conjunctival fornix. The pattern of staining with rose bengal was evaluated. The area examined was the

interpalpebral area, and each eye was divided into 3 zones a medial, central corneal and lateral. Each field received a score that subsequently was summarized according to van Bijsterverd scoring method. Van Bijsterved 1 point, referred to the staining of single points, 2 points was referred to a scattered pattern and 3 points staining of confluent areas of the ocular surface. In this way each eye received a maximum score of 9 if it stained maximally in all 3 zones. A score of more than 3 points of the van Bijsterverd were considered as pathological. The patients with pingueculae or pterygium were excluded, as these lesions do give false positive results. The score for each eye were recorded and analysed separately.

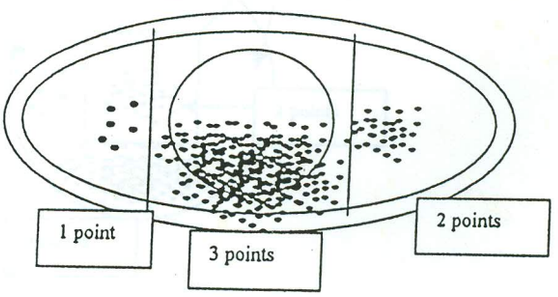


FIG. 1 Rose bengal staining of the conjunctiva and cornea (Bijsterverd score). 1 point, single pattern, 2 points, scattered and 3 points, confluent staining.

Fluorescein stain test.

Fluorescein dye stains the cornea or conjunctiva surface if the epithelial integrity is compromised. Fluoret strip was put into the lower conjunctival fornix of the eye to be examined. The patient was asked to blink 3 times to distribute the dye. Using the slit lamp patients were examined under blue filter observing the fluorescein staining of the cornea. The fluorescein staining of the cornea was investigated by dividing the cornea into five parts. One to three points were given. 1 point, referred to the staining of single patterns, 2 points, staining of scattered dots, 3 points confluent areas within each five sections. Staining score points of each division were summed up to 15 maximum points if they stained maximally. Score of more than 3 points was regarded as pathological.

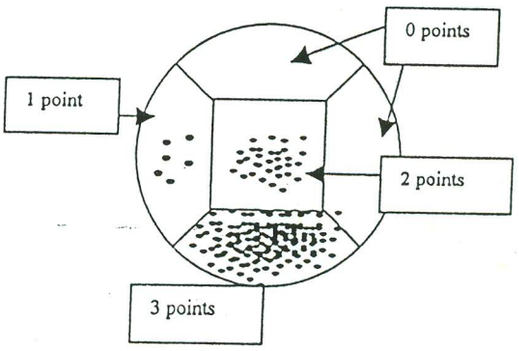


FIG.2. Fluorescein staining of the cornea. The cornea is divided into five parts. One to three fluorescein points are given. 1 point, staining of single pattern, 2 points, staining of scattered dots and 3 points, confluent staining. Staining points of each division are summed for 15 maximum points.

Statistical data analysis: Data collected was entered into the statistical data package of Epi-Info 6 version. During analysis patients were grouped into three age groups, 20-39, 40-59 and 60 years and above. Comparison between proportions were made using chi- square test for categorical variables. Differences between variables were considered significant if p value was less than 0.05.

RESULTS

For a period of one year (February 2000 to January 2001) two hundred patients with eyelid, conjunctival, and corneal inflammatory diseases were studied. The age range of the subjects studied was 20-82 years with a mean of 37.8 years and median of 32 years. The sex distribution was 61 (30.5%) males and 139 (69.5%) females giving a male: female ratio of 1:2.3. The majority of patients in all age groups were females. Of the 200 patients 126(63.0%) were in the age group 20-39 (Table1).

Table 1:Distribution of the study population by age and sex

Age (years)	Male	Female	Total
20-39	41(32.5%)	85(67.5%)	126(100.0%)
40-59	13(27.0%)	35(73.0%)	48(100.0%)
60+	7(26.9%)	19(73.1%)	26(100.0%)
Total	61(30.5%)	139(69.5%)	200(100.0%)

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Schirmer test 1 was used to measure tear secretion. The results indicated that 14 (7%) of the study population had dry eyes. Tear secretion was significantly lower in the age group 60 years and above compared to the younger age groups (Table 2).

Table 2: Frequency distribution of tear secretion by age

	Age(years)			
Tear secretion	**20-39**	**40-59**	**60+**	**Total**
≤5mm\5min	6(4.8%)	1(2.1%)	7(27.0%)	14(7.0%)
>5mm\5min	120(95.2%)	47(97.9%)	19(73.0%)	186(93.0%)
Total	126(63.0%)	48(24.0%)	26(13.0%)	200(100.0%)

χ^2 = 18.6, df=2, p value<0.00001

A large proportion of females (7.9%) had low tear secretion compared to males (4.9%). This difference however was not statistically significant (p value=0.64, table3).

Table 3:Distribution of tear secretion by sex

Tear secretion	**Male**	**Female**	**Total**
≤5mm	3(4.9%)	11(7.9%)	14(7.0%)
>5mm	58(95.1%)	128(92.1%)	186(93.0%)
Total	61(100.0%)	139(100.0%)	200(100.0%)

X^2_{yates}=0.21, df=1, p=0.64

The hallmark of dry eye is unstable tear film, which was also evaluated. The prevalence of dry eye by tear break-up time was 40 (20%) of the study subjects. The tear stability significantly decreased with increasing age (p value= 0.04, table4).

Table 4:Distribution of tear stability by age

	Age(Years)			
Tear stability	20-39	40-59	60+	Total
≤10seconds	21(16.7%)	9(18.8%)	10(38.5%)	40(20.0%)
>10seconds	105(83.3%)	39(81.2%)	16(61.5%)	160(80.0%)
Total	126(100.0%)	48(100.0%)	26(100.0%)	200(100.0%)

X^2=6.46, df=2, p=0.04

More males (21.3%) than females (19.0%) had low tear stability. However this difference was found not to be statistically significant (p value=0.76, table5).

Table 5:Distribution of tear stability by sex

Tear stability	**Male**	**Female**	**Total**
≤10 seconds	13(21.3%)	27(19.0%)	40(20.0%)
> 10 seconds	48(78.7%)	112(81.0%)	160(80.0%)
Total	61(100.0%)	139(100.0%)	200(100.0%)

X^2=0.09, df=1, p=0.76

Visual acuity was classified according to World Health Organization criteria for visual impairment.184 patients (92%) had a corrected visual acuity in one or both eyes of ≥6/18, 14 (7%) had <6/18 to 6/60 vision, and 2 (1%) had <6/60 to 3/60 vision. Thus 92% of the study population had normal vision, 16(8%) had visual impairment but no patient was found to be blind (Table 6).

Table 6:Visual acuity distribution of the study population

Visual acuity (corrected)	**No**	**%**
≥6/18	184	92.0
<6/18 - 6/60	14	7.0
<6/60 - 3/60	2	1.0
<3/60 -1/60	0	0.0
<1/60 - LP	0	0.0
NLP	0	0.0
Total	200	100.0

When comparing visual impairment between patients with low tear secretion and those with normal tear secretion, 57.1% of the patients with low secretion had visual impairment, whereas only 4.3% of the patients with normal tear secretion had visual impairment (Table7).

Table 7:Distribution of visual acuity by tear secretion

Visual acuity	**Tear secretion**		
(Corrected)	**≤5mm**	**>5mm**	**Total**
≥6/18	6(42.9%)	178(95.7%)	184(92.0%)
<6/18 – 6/60	6(42.9%)	8(4.3%)	14(7.0%)
<6/60 – 3/60	2(14.2%)	0(0.0%)	2(1.0%)
Total	14(100.0%)	186(100.0%)	200(100.0%)

Among patients with low tear stability 22.5% had visual impairment, whereas only 4.4% of those patients with normal tear stability had visual impairment. The results are only marginally significant (p value= 0.04, table 8).

Table 8:Distribution of visual acuity by tear stability

Visual acuity (Corrected)	Tear stability ≤10seconds	>10seconds	Total
≥ 6/18	31(77.5%)	153(95.6%)	184(92.0%)
<6/18 - 6/60	8(20.0%)	6(3.8%)	14(7.0%)
<6/60 - 3/60	1(2.5%)	1(0.6%)	2(1.0%)
Total	40(100%)	160(100.0%)	200(100.0%)

$\chi 2$=6.46, df=2, P-value= 0.04

When the tear secretion and tear stability were analysed and compared, there was a significant association between tear secretion and tear stability. Among patients with low tear stability (64.3%) had low tear secretion compared to (35.7%) of those with normal tear stability (p value< 0.0001, table 9).

Table 9:Distribution of tear secretion by tear stability

	Tear stability		
Tear secretion	**≤10seconds**	**>10seconds**	**Total**
≤5mm\5min	9(64.3%)	5(35.7%)	14(100.0%)
>5mm\5min	31(16.7%)	155(83.3%)	186(100.0%)
Total	40(20.0%)	160(80.0%)	200(100%)

χ^2_{yates} =15.60 df=2, P value <0.0001

Of the 40 patients who had low tear stability 31 (77.5%) had normal tear secretion (Table10).

Table 10:Distribution of tear secretion among 40 patients with low tear stability.

Tear secretion	**No**	**%**
≤5mm\5min	9	22.5
>5min\5min	31	77.5
Total	40	100.0

The severity of ocular surface damage was evaluated by rose bengal and fluorescein stains. By rose bengal stain, 182 (91%) patients had a van Bijsterveld score between 0-3 and 18 (9%) of the patients had a score of more than 3. Thus the prevalence of dry eye by rose bengal stain was 9% (Table11).

Table 11:Distribution of ocular surface staining by rose bengal stain

Van Bijsterveld score	No	%
0-3	182	91.0
> 3	18	9.0
Total	200	100.0

The prevalence of dry eye by using fluorescein corneal stain was 14 (7%) (Table12).

Table 12:Distribution of ocular staining by fluorescein stain

Fluorescein staining	No	%
0-3 score	186	93.0
> 3 score	14	7.0
Total	200	100.0

Soreness, sandy like sensation, blurred vision and morning burning pain were symptoms reported most by patients with low tear secretion. The prominent symptoms among patients with normal tear secretion were itching, tearing, soreness and sandy like sensation (Table 13).

Table 13:Distribution of symptoms by tear secretion

Symptoms	**≤5mm N=14**	**>5mm N=186**
Sandy sensation	10(71.4%)	104(55.9%)
Morning pain	8(57.1%)	37(19.9%)
Blurred vision	7(50.0%)	34(18.3%)
Soreness	9(64.2%)	114(61.3%)
Tearing	3(21.4%)	110(59.0%)
Itching	4(28.6%)	126(67.7%)

Symptoms felt most by patients who had normal tear stability were itching, tearing, soreness and sandy like sensation. Sandy like sensation, soreness, blurred vision and burning pain were the symptoms felt most by patients with low tear stability (Table 14).

Table 14:Distribution of symptoms by tear stability

Symptoms	≤10 seconds N=40	>10 seconds N=160
Sandy sensation	32(80.0%)	89(55.6%)
Morning pain	20(50.0%)	34(21.2%)
Blurred vision	16(40.0%)	24(15.0%)
Soreness	29(72.5%)	96(60.0%)
Tearing	9(22.5%)	100(62.5%)
Itching	12(30.0%)	109(68.2%)

The diseases associated with dry eye were trachoma, xerophthalmia, herpes zoster ophthalmicus and Steven-Johnson syndrome. Only 4 out of 125 patients with allergic conjunctivitis had dry eye. I7 (8.5%) had dry eye without any associated systemic or ocular disease (Table15).

Table15: Distribution of study group by systemic and ocular diagnosis

Diagnosis	No	%
Steven-Johnson syndrome	7	3.5
Herpes zoster Ophthalmicus	12	6.0
Blepharitis	5	4.5
Trachoma	17	8.5
Xerophthalmia	6	3.0
Allergic conjunctivitis	125	62.5
Mooren's ulcer	4	2.0
Skin onchocerciasis	1	0.5
Corneal dallen	3	1.5
Dry eye	17	8.5
Chemical burn	3	1.5
Total	200	100.0



DISCUSSION

Most of the studies done on prevalence of dry eye were large scale and community based.[3,4,14,15,16] Most of the available data is based on studies done in developed countries. The diagnosis of dry eye in these large scale studies was mainly based on reported symptoms.[3,14,15,16,17] The current study is a hospital-based study. This difference does affect the comparability of results of this study and the previous reports. In this study the prevalence of dry eye varied depending on the test used to diagnose dry eye. The prevalence by Schirmer was 7%, 20% by tear break up time, 9% by rose bengal, 7% by fluorescein stain and 4.5% had both low tear secretion and tear stability. These findings are comparable with results of other reports.[3,4]

In reports of previous studies, females comprised the majority of patients and were reporting more dry eye symptoms than males.[4,14,95] In the Beaver Dam study this difference persisted in all age groups.[14] In this study females also comprised the majority of patients with eyelid, conjunctival and corneal inflammatory diseases. Females were also the majority in all the age groups. Therefore, the results of this study agree with the previous studies.[4,14,95] There is no easy explanation why there were more females in the current study. Probably this could be associated with the use of cheap cosmetics. The use of cosmetics among females in Tanzania is very high.

However there are no studies done to evaluate the association of cosmetics and eye irritation or inflammation.

Schirmer I test is a good simple clinical test to assess tear secretion. However, false positive and false negative results occur in 15% of eye tested.[2,97] But a persistent repeated reading of less than 5mm of wetting in one or both eyes is an indication of low tear secretion.[10,11] The Melbourne study,[4] which used symptoms and diagnostic tests in diagnosing dry eye found the prevalence of dry eye by Schirmer test (cut off point<8mm) to be 16.3%. The Salisbury study which used cut off point of <5mm reported that 2.2% of patients were symptomatic and had low tear secretion.[3] This study using cut off point of ≤5mm found 7% of symptomatic patients had low tear secretion. This difference from the Melbourne study can be explained by the difference in the age of the study groups. The Melbourne study population was older with a mean age of 59 year whereas with the current study the mean age was 39 years. Another reason is the difference in the cut off points. The Melbourne study used a higher cut off point, which might have contributed to the high prevalence. The prevalence of 7% appears high as compared to the Salisbury study.[3] This can be explained by the fact that Salisbury study was a community based while this study was a hospital based study and was expected to be a biased sample of symptomatic cases.

The results of previous studies noted that tear secretion decreased with advancing age.[4,14,96,98,99,100,101] This is a result of normal aging changes occurring in tear producing glands. Advancing age tends to result in gradual decline of tear production.[98,99,100] Reduction of the tear volume, flow and increased evaporation has been noted in older people.[42] Age also is associated with a decline in corneal sensation. Studies have suggested that in old age there is increased evaporation and subsequent increase in tear osmolarity.[66] With increasing age there is increased lacrimal and meibomian gland dysfunction.[12] The results of this study do not differ much from previous studies, as the tear secretion decreased significantly in those aged 60 years and above (p.value <0.0001). Although the tear stability decreased with increasing age, the statistical significance was only marginal (p. value 0.04). The most likely reason is that, this study recruited more young patients. The majority of the study subjects were in the age between 20-39 years, whereas in most previous reports, the study subjects were 40 years old and above.[3,4,15,16,17]

Dry eye has been noted to be a major problem among elderly female patients with symptoms of eye irritation.[4,14,95] It has been documented in the literature that females comprise the majority of patients with aqueous deficiency dry eye.[49] The trouble appears to begin during menopause when oestrogen and androgen levels decline.[45,46,47] This is supported by a significantly increased incidence

of dry eye in women.[4,14] Studies have shown that sex hormone appear to modulate aqueous tear output, lipid production, mucin secretion and tear film stability.[45,46,47] In this current study, there were more femalesthanmales. However this finding was not statistically significa nt. The results comparably agree with the results of the Salisbury study, which also reported no significant association of low tear secretion and sex.

In dry eye, the tear film loses water either through decreased tear production or increased tear evaporation.[7] On cellular level, the first change that occurs is a decrease in conjunctival goblet cells. [7,60] As a result, there is less mucin and less natural lubrication of the eye and hence tear instability.[7] The major cause of mucin deficiency is hypovitaminosis A, which is a public health problem in developing countries.[61] Vitamin A deficiency produces uneven wetting of the corneal surface, resulting in unstable tear film. Other conditions that, do contribute in tear instability in developing counties are conditions like chemical burn, Steven-Johnson syndrome and trachoma.[2,61] Studies done to evaluate the importance of the lipid layer, have found that tear break-up time varies significantly with lipid layer abnormality.[24 34] They found when lipid layer was absent the tear film was unstable. Studies done in United States and Japan have demonstrated that meibomian gland disease is a very common clinical condition involving approximately 60% to 80% of all dry eye

patients.[42,43,102,103,104] The prevalence of dry eye by tear break-up time in this study was 20% (cut off point of ≤10), where-as the Melbourne study found the prevalence of dry eye by tear break-up time to be 8.6% with a cut off point of < 8 seconds. The explanation is not straight forward, but the difference in cut off points might account for the difference in the prevalence of these two studies. Also prevalence of 20% appears high and probably reflects, the fact that this was a biased sample of symptomatic patients. Another reason is that this study did not evaluate the lipid layer. It is also possible some of these patients had coexisting lipid layer deficiency, which has been found to be significantly associated with low tear break-up time.

Precorneal tear film has several functions. The important optical function is to smoothen out the irregular surface of the cornea, providing better refracting surface. The integrity of the precorneal tear film is essential for maintaining a good vision and ocular comfort.[2,6,9,21] Experiments have shown removal of precorneal tear film results in an alteration of corneal barriers function to fluorescein dye and increased corneal irregularity.[105,106,107,108] Dry eye in its mild form may only cause irritation but a severe form can be detrimental to vision.[2,9] The cause of poor vision could be corneal scaring, neovascularization, formation of symblepharon, sterile corneal ulcers that rapidly perforates, and keratinisation of corneal epithelium.[2,6,9] The causes of poor vision in this study were corneal scarring,

vascularization, extensive corneal filaments and epithelial keratinisation. In a study done in Pakistan among 30 patients with dry eye 50% were blind, 20% had visual impairment and only 30% had normal vision.[17] However from the results of this study, 184(92%) of the study population had normal vision, 16(8%) had visual impairment but no patient was found to be blind. When comparing the visual impairment between patients with normal tear secretion and those with low tear secretion, eight (57.1%) patients with low tear secretion had visual impairment whereas in those patients with normal secretion the visual impairment was only 4.3%. Visual impairment in patients with low tear stability was 22.5% while in the patients who had normal tear stability it was only 4.4%. This signifies that visual impairment among patients with dry eye is high and supports the results from Pakistan.[17]

Several studies reported a significant correlation between tear stability and tear secretion.[43,96,109] It has been reported that tear break-up time is short in acqueous tear deficiency and is always shortest in eyes with mucin layer deficiency.[95] The primary function of mucin is to coat the surface of the corneal epithelium and thus render it wettable by the aqueous tears.[9,95] In a previous study done in patents with dry eye comparing tear secretion and tear thinning found a correlation between them.[1109] The study demonstrated that 14.7% of the patients had normal tear thinning and low tear

secretion. Patients who had low tear stability and normal tear secretion accounted for 14.7% of the dry eyes. Patients who had both low tear secretion and stability comprised 70.6% of the dry eyes (cut-off point of11.31mm 9.8 seconds respectively). This study used the findings to classify dry eyes into three types. Type A with normal tear stability and low tear output. Type B, with low tear stability and normal output and a type C with low stability and low output. In the present study the association between tear secretion and tear stability was evaluated and the results were statistically significant. Among 14 patients who had low tear secretion, 9(64.29%) of them had low tear stability and 5(35.71%) the tear secretion was normal. Patients who had normal tear stability and low tear secretion comprised 2.5% of the study population. Patients who had low tear secretion and normal tear stability comprised15.5%, whereas those with both low tear secretion and stability accounted for 4.5% of the study population. Among the patients who had low tear stability 77.5% had normal tear secretion.

Rose bengal stain provides a direct evaluation of epithelial cell damage and is an indirect measurement of tear volume deficiency.[2,9] Rose bengal also stains mucin and filaments which are often prominent findings in dry eye conditions.[2,9] In this study the prevalence of dry eye by rose bengal was 9%. This compares favourably with the Melbourne study, which reported the prevalence

of dry eye based on rose bengal to be 10.8%. However, the results of this study differs very much from the community based Salisbury study which found the prevalence of dry eye by rose bengal to be 2%.[2] The difference can be accounted for probably by the difference in the cut off points. The Salisbury study used a cut off point of ≥5 score while this study used a cut off point of >3.

The prevalence of dry eye by fluorescein stain found by this study was 7%. This differs from the Melbourne study, which had a prevalence of 1.5%. As stated previously, the current study was a hospital based and had a small sample size. The cases seen seem to be over represented, while the Melbourne study was a community based study and revealed the actual prevalence in that community.

It has been documented in the literature that patients with dry eye of different causes usually have similar complaints.[9 21] The symptoms vary from blurred vision, burning pain, soreness, tearing, itching and photophobia.[2,9,39] The patients evaluated by this report had three or more concurrent symptoms. The symptoms reported most in patients who had low tear stability and or low tear secretion were sandy like sensation, blurred vision, soreness and burning pain. Prominent symptoms felt by patients who had normal tear secretion and or normal tear stability were itching, tearing, soreness and sandy like sensation. The majority of patients with negative tests were suffering

from allergic conjunctivitis. The symptoms compare well with those documented in the literature.[2,9]

In this study trachoma, Stevens Johnson syndrome, herpes zoster ophthalmicus and xerophthalmia were the diseases found to be associated with dry eyes. This is because xerophthalmia and trachoma are still public health problems in Tanzania.[2,50,51] Four patients with Xerophthalmia were prisoners. The majority of patients who had herpes zoster ophthalmicus or Stevens-Johnson syndrome were also seropositive for HIV, which is also a public health problem in developing countries. One patient, a soldier from Morogoro had cutaneous onchocerciasis with dry eyes. This patient had generalised skin nodules, which were very itchy. It is difficult to explain the association of onchocerciasis with dry eyes as no case has been reported in the literature.

The results of this hospital-based study cannot provide the exact information on the magnitude of dry eye in the community. However, it has highlighted that dry eye is a problem among patients with ocular irritation and inflammation. The study has emphasized the importance of diagnostic approach to dry eye. The use of both symptoms and diagnostic tests in the diagnosis of dry eye states is important and was applied in the study. This approach was considered because it has been reported that there is no individual test, which can adequately diagnose disorders of tear film.[7,12,66,96,97]

Each test examines only part of the tear disturbance and it is only when these tests are employed collectively that a more complete picture of the tear film is obtained.[110] In that way the study has fulfilled the recommendation of the National Eye Institute/Industry workshop on Clinical Trials in Dry Eye.[7] The workshop developed a global definition of dry eye and listed criteria for diagnosis of dry eye. The criteria included symptoms, interpalpebral surface damage, tear instability and tear hyperosmolarity.[7]

Conclusion and recommendation

Dry eye is prevalent among patients with eyelid, conjunctival and corneal inflammatory diseases in Dar es salaam and the prevalence varied depending on the diagnostic tests used.

1.Community based studies need to be done to get the exact prevalence of dry eyes in the community.

2.The approach of using several diagnostic tests to get the complete picture of dry eyes is recommended.

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