"A ONE YEAR CROSS SECTIONAL STUDY OF DRY EYE IN RHEUMATOID ARTHRITIS PATIENTS AT KLES DR. PRABHAKAR KORE HOSPITAL & MEDICAL RESEARCH CENTRE, BELGAUM"

by

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Dissertation

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MASTER OF SURGERY (M.S.)

in

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Under the Guidance of

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It takes time to succeed because success is merely the natural reward of taking time to do anything well.

- Joseph Ross

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Dr. Chaitra K.L.

LIST OF ABBREVIATIONS

χ^2	Chi squared test
H & E	Haematoxilin and Eosin
HLA	Human Leukocyte Antigen
IL	Interleukin
N:C	Nuclear Cytoplasmic ratio
NS	Not significant
OSDI	Ocular Surface Disease Index
PAS	Periodic acid Schiff
QoL	Quality of life
RA	Rheumatoid arthritis
RF	Rheumatoid factor
S	Significant
ST	Schirmer test
TBUT	Tear film Break Up Time
TNF	Tumor Necrosis Factor

ABSTRACT

Background and objectives:

Dry eye is a very common disorder of tear film resulting from either decreased tear production or increased tear evaporation. It is not a common cause of vision loss, but it is still a serious issue for people who have it. The symptoms become progressively troublesome and exert an increasing burden on the patients as the disease progresses or increases in severity. If not detected early, it can lead to sight threatening complications. Rheumatoid arthritis is a well known risk factor for dry eye occurrence. This study was undertaken to assess dry eye prevalence in rheumatoid arthritis patients.

Methods:

The study was conducted at J.N.Medical college , Belgaum for a period of one year (January 2007 to January 2008). 70 patients diagnosed to have rheumatoid arthritis were enrolled in this study. They were given an OSDI questionnaire, examined for signs of dry eye and subjected to four tests (Schirmer test, Tear film break up time, rose bengal test, Impression cytology), based on which they were labelled as being positive or negative for dry eye.

Results:

Dry eye prevalence was found to be as high as 48.5% among rheumatoid arthritis patients. High OSDI scores were found to correlate well with diagnostic tests done for dry eye. The occurrence of dry eye was found to be more among females and people with refractive errors. Prevalence was found to increase with the increase in

age and increase in duration of rheumatoid arthritis. A significant number of patients also had evidence of dry mouth. There was no correlation between rheumatoid factor and occurrence of dry eye.

Conclusion:

Rheumatoid arthritis is a definite risk factor for occurrence of dry eye. Testing in patients of rheumatoid arthritis is essential to detect dry eye early in these patients. OSDI questionnaire is a useful screening tool for dry eye. Impression cytology is an easy and useful test to assess surface changes in dry eye patients. While testing for dry eye, other criteria such as patient's age, sex, refractive error, duration of rheumatoid arthritis should also be taken into consideration.

Key words:

Dry eye, Rheumatoid arthritis, OSDI, Impression cytology.

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INTRODUCTION

Rheumatoid arthritis is the most common rheumatic disorder affecting approximately 1% of adults. It is classically an additive, deforming, symmetrical, peripheral polyarthritis characterised by inflammation of synovial membrane. Though all joints may be involved, it primarily affects the small joints of hands and feet. It shows gel phenomenon i.e. stiffness at rest which improves with movement. About 80% of the patients with RA are positive for rheumatoid factor, which is an autoantibody directed against immunoglobulin G. This is a multisystem disease with wide extra articular manifestations. Ocular manifestations form a part of the extra articular manifestations of rheumatoid arthritis.

Ocular manifestations of rheumatoid arthritis include keratoconjunctivitis sicca, episcleritis, scleritis and corneal melting. Dry eye has been found to be the commonest ocular manifestation of rheumatoid arthritis. Such patients, having both rheumatoid arthritis and dry eye are labelled as having secondary Sjogren's syndrome.[1]

Dry eye is a very common disorder of tear film resulting from either decreased tear production or increased tear evaporation. The tear film becomes unstable with loss of water and progressive deterioration of ocular surface ensues. Surveys over the last 20 years have estimated the prevalence of dry eye disease to be between 5% to more than 50% at various ages and with various risk factors.[2]

People with dry eye syndrome are bothered by irritative ocular symptoms which can be likened to other chronic pain syndromes where in such ongoing

problems may also lead to a general sense of ill health or psychological comorbidities. The poor correlation between the signs and symptoms of dry eye has lead to a necessity for performing diagnostic procedures on patients at risk for developing dry eye, in order to diagnose the condition at an early stage.

Patients often delay seeking care for their dry eyes until the tissue damage is at a more advanced stage. Early medical intervention to arrest the RA-associated damage to the lacrimal glands may preserve healthy moisture levels to the ocular surface and protect the eyes from long-term damage. An accurate knowledge of the prevalence of dry eye in rheumatoid arthritis will increase the case detection rate of dry eye in these patients, thus improving their quality of life.

AIMS AND OBJECTIVES

1) To determine the prevalence of dry eye in patients of rheumatoid arthritis.

2) To study the association between chronicity of rheumatoid arthritis and presence of dry eye.

3) To study the association between RA factor and dry eye occurrence.

REVIEW OF LITERATURE

The tear film is a dynamic structure that is produced by and affecting the adjacent living tissue. These two structures are interrelated. The maintenance of a normal tear film depends on the maintenance of a normal ocular surface. Similarly, the ocular surface cannot retain its normal structure in the absence of a normal tear film. Hence, a study of both these structures is important to understand the mechanism and effects of dry eye.

OCULAR SURFACE:

Anatomy:[3]

The bulbar conjunctiva is a thin and translucent structure. It is tied to the subjacent structures by areolar tissue and is mobile to allow ocular movements. The conjunctival structure varies from region to region and also differs with age. The neonatal conjunctiva is pristine.

Conjunctival *epithelium* consists of different layers. The deepest layer consists of cylindrical cells (as in epidermis), with intermediate layers of polyhedral cells. The most superficial layer is flat but indented. Goblet cells are absent at muco-cutaneous junction, begin to appear and are very numerous beyond the sub tarsal folds. From the fornix to limbus, the epithelium becomes less glandular, losing its goblet cells, and more epidermal in type, but never keratinized. At the limbus, the epithelium is stratified and papillae form, giving the deep aspect a characteristic sinuous profile.

Goblet cells are most dense nasally, least dense in the upper temporal fornix and absent at the palbebral muco cutaneous junction and limbus. They are chief

source of mucin. They arise from basal layer of epithelium and tend to retain attachment to its basement membrane. They are round to oval in shape, 10-20µm wide, with flat basal nuclei. Cells become larger and more oval as they approach the surface where they develop a stoma and discharge their mucin content. Electron microscopy shows that they are attached by desmosomes to the neighbouring epithelial cells. The density of goblet cells is 10±3 cells/mm^2.

Cytology:[4]

Bulbar conjunctiva is composed of stratified columnar epithelium. The cells are round, pyramidal or elongated cylindrical measuring 15-25µ in diameter.

Cytoplasm is semitransparent, adequate to abundant. It stains blue green with papinicolou stain. Border is well defined, sharp and regular. Some cells may have intracytoplasmic, orange brown melanin granules. No cilia or terminal bars are present.

The nucleus is single, round to oval, eccentric, measuring 6-9µm in diameter. It has smooth regular nuclear membrane and moderately course granular chromatin that is uniformly distributed. Nucleolus is single, small, red and round.

TEAR FILM:

Anatomy:[5]

The pre ocular tear film is the sheet of tears which covers the exposed interpalpebral portion of the globe and the cornea. Thickness of the tear film is 40µm.

It consists of 3 layers:

The superficial oily layer is derived from meibomian glands and accessory sebaceous glands of Zeis. It reduces the rate of evaporation of the underlying tear layer, forms a barrier along the lid margin tear strip and prevents its outflow onto the skin. It is 0.1µm thick. Chemically, this layer consists of lipids having low polarity, such as wax and cholesterol esters. With dim illumination & using the tear film as a mirror surface, this layer may be seen as multicoloured interference pattern.

The middle aqueous layer is secreted by the lacrimal gland and the accessory glands of Krause and Wolfring. The main bulk of thickness of tear film is constituted by this layer. Thickness is uniform over the cornea and varies between 6.5µm and 7.5µm. It is an aqueous solution of low viscosity containing inorganic salts, glucose, urea, biopolymers, proteins and glycoproteins. The constituents are added by all the glands which abut the conjunctival sac.

The mucoid layer, is said to be bonded to the glycocalyx of the surface epithelial cells. It measures 0.02 to 0.05 µm in size. It is demonstrable in the living eye by Alcian blue drops instilled in the tear sac and in the ultrastructural studies by staining with Ruthenium red and other dyes.

The innervational control of tear secretion is derived from 3 sources- trigeminal nerve, facial nerve, cervical sympathetic nerves.

Average tear flow is about 1.2µl/min.

Distribution of tears: Tears are found in the conjunctival fornices (4.5µl), pre ocular tear film (1.1µl) and along the marginal tear strip (2-9µl). The marginal tear strips are

wedge shaped tear menisci which run along the posterior borders of upper and lower lids at their points of apposition to the globe. By staining the tears with fluorescein, the marginal tear strips may be demonstrated using a blue light source. The normal height of tear menisci is 1 mm.[6]

Role of blinking: The preocular tear film is compressible and elastic. It has clinging properties that preserve its stability and spreading properties that ensure clear vision immediately after blinking. In the act of blinking, the upper lid descends & the marginal strip of tears sweeps over the cornea. Goblet cells of tarsal conjunctiva release mucus which coat its smooth surface and spread a mucin layer on to the surface of corneal epithelium. Normal blink rate is approximately 15-18 blinks/min. Each blink lasts 0.3 seconds. The rate is higher for men compared to women. It increases with emotional outbursts or anxiety states. The rate may go down by 60% in a tired blinker, with reading, driving or watching computer screens during the full working day.[7]

Composition:[5]

It is composed of 3 protein fractions- albumin, globulin and lysozyme.

The immunoglobulins found in normal tear fluid are IgA, IgG, and IgE. IgA predominates in the secretory form. Lysozyme acts synergistically with the IgA in causing the lysis of bacteria. Tears also contain lactoferrin, which has some antibacterial effect. In addition, it also contains electrolytes such as Na, K and Cl in higher concentration than blood.

The average pH of tears is 7.25

Osmolality is 309mOsm/l

Surface tension is 40-42mN/m

Refractive index of tear film is 1.336.

Functions:

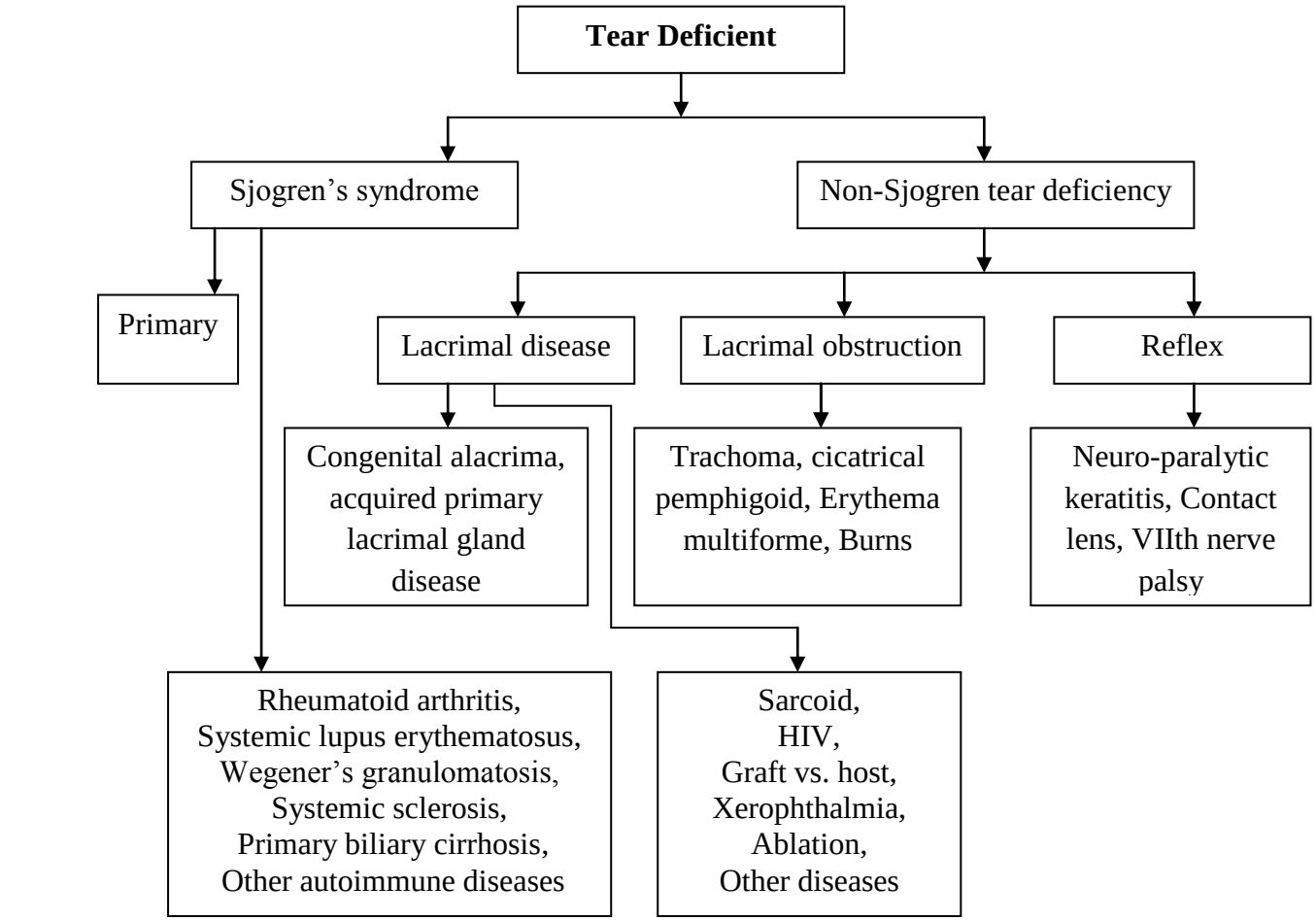
1) It makes the cornea a smooth optical surface.
2) It flushes out the debris and organisms from the corneal surface.
3) It has bactericidal properties due to the presence of lysozyme, lactoferrin and betalysin.
4) Immunoglobulins and specific antibodies in the tears defend the eye against external infections
5) Lubricating action of tear film minimizes the frictional trauma between tarsal and bulbar conjunctiva and cornea.
6) It provides epithelial cells with glucose, oxygen and growth factors.

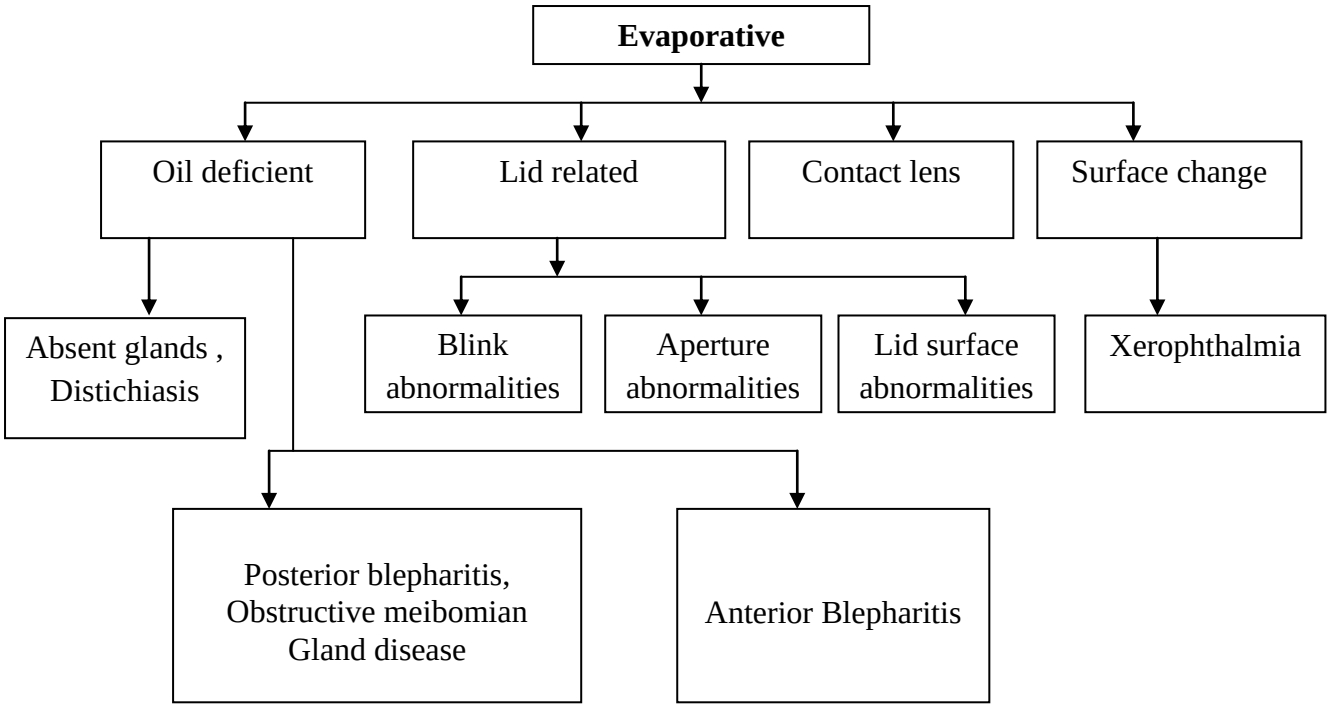
DRY EYE:

The clinical condition that results when tear production is decreased or when excessive loss of tear film results from evaporation, is known as dry eye. In December 1993 and 1994, the National Eye Institute industry workshops were held, to give a common definition and guidelines regarding management of dry eye.[8] They came up with the following definition of dry eye. **" Dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort**".[9]

Classification:

Dry eye has been classified into 2 main varieties by Holy and Lemp- i.e *tear deficient* and *evaporative* forms of dry eye.[8]


Tear Deficient
Sjogren's syndrome
Non-Sjogren tear deficiency
Primary
Lacrimal disease
Lacrimal obstruction
Reflex
Congenital alacrima, acquired primary lacrimal gland disease
Trachoma, cicatrical pemphigoid, Erythema multiforme, Burns
Neuro-paralytic keratitis, Contact lens, VIIth nerve palsy
Rheumatoid arthritis, Systemic lupus erythematosus, Wegener's granulomatosis, Systemic sclerosis, Primary biliary cirrhosis, Other autoimmune diseases
Sarcoid, HIV, Graft vs. host, Xerophthalmia, Ablation, Other diseases


Evaporative
Oil deficient
Lid related
Contact lens
Surface change
Absent glands , Distichiasis
Blink abnormalities
Aperture abnormalities
Lid surface abnormalities
Xerophthalmia
Posterior blepharitis, Obstructive meibomian Gland disease
Anterior Blepharitis

As shown in the flow chart, rheumatoid arthritis forms one of the causes of tear deficient type of dry eye and is labelled as a type of secondary Sjogrens syndrome.

RHEUMATOID ARTHRITIS:

Rheumatoid arthritis (RA) is a chronic, immuno inflammatory, systemic disease that affects mainly synovial joints with possibility of extra articular manifestations. Generally the joint involvement is bilateral, peripheral, symmetrical, characterized by early morning stiffness with a positive rheumatoid factor in approximately 75% of patients.[10] The prevalence of RA is approximately 0.8% in general population (range 0.3-2.1%); women are affected 3 times more often than men. The prevalence increases with age, and sex differences diminish in the older age group. RA is seen throughout the world and affects all races. The onset is most frequent during the fourth and fifth decades of life, with 80% of all patients developing the disease between the ages of 35 and 50 years.

Pathogenesis:[11]

Data collected over the last decade clearly indicate that the disease mechanisms are much more complex than previously thought. More than one pathologic event is involved in the tissue destructive response. Detailed studies on the contribution of HLA polymorphism in the disease process have challenged the idea that these molecules regulate the disease initiation. Rather, their pivotal role seems to be in modulating the disease course, determining the disease progression and influencing the clinical pattern of the disease.

Initial studies into immunologic dysfunction in RA patients were focussed on autoantibody production, particularly RF production. Indeed, the hypothesis that RA is an autoimmune disease was entirely driven by the consideration that autoreactive antibody molecules are disease inducing. The realization that T cells have a pivotal role in regulating immune responses & the observation that T cells accounted for the dominant tissue infiltrating cell type shifted the emphasis towards studies of T cell function. Further studies are going on to understand the molecular mechanism in this condition.

Diagnostic criteriae: [10]

The American College of Rheumatology(ACR) criteria is widely followed for diagnosis and classification of rheumatoid arthritis. The criteriae are-

Morning stiffness : In and around the joints, lasting at least 1 hour before improvement

Arthritis of 3 or more joint areas : At least 3 joint areas simultaneously have soft tissue swelling or fluid observed by a physician. Areas are, PIP, MCP, wrist, elbow, knee, ankle and MTP joints.

Arthritis of hand joints: At least one area swollen (in a wrist, MCP or PIP joint).

Symmetric arthritis : Simultaneous involvement of same joint areas on both sides of the body.

Rheumatoid nodules: Over bony prominences, or in juxta articular regions.

Serum rheumatoid factor: Demonstration of abnormal amounts of serum rheumatoid factor by any method for which result has been positive in 55% of normal control subjects.

Radiographic changes: include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints.

For a person to be labelled as having rheumatoid arthritis, atleast 4 of the 7 criteria should be satisfied and criteria 1 to 4 should be present for atleast 6 weeks.

Rheumatoid factors are antibodies directed against the Fc portion of immunoglobulin G (IgG). A positive test for rheumatoid factor is by no means pathognomonic of rheumatoid arthritis, but is present in 70 to 90% of patients with the disease. The titre does not correlate with the activity of disease, but patients with a high titre rheumatoid factor are more likely to have erosive joint disease, extra-articular manifestations, and greater functional disability. In contrast, generally, rheumatoid factor negative patients exhibit a milder disease course. Hence they are of prognostic value. Rheumatoid factors are also detectable in non-rheumatoid patients who have chronic antigenic stimulation, such as prolonged infection (bacterial endocarditis, tuberculosis, cytomegalovirus, human immunodeficiency virus (HIV), collagen vascular disease, or dysproteinemia. Low titres of rheumatoid factors may be detected in the serum of apparently normal people, especially over the age of 70, where its prevalence is anywhere from 10 - 25%.[12] The anti-nuclear antibody (ANA) is positive in 20-30% of patients with rheumatoid arthritis and is more common in patients with extra-articular manifestations.

Extra articular manifestations:

It is estimated that as many as 40% of patients may have extra articular manifestations and in approximately 15%, these are severe. A study done in 1997 to assess the incidence of extra articular manifestations among Indian population, found that the duration of disease was longer and rheumatoid factor positivity higher in those with extra articular manifestations compared to those without. They also found that the incidence of extra articular manifestations was the same compared to western population.[13]

Ocular manifestations:

Ocular manifestations form an important part of extra articular manifestations of rheumatoid arthritis. The parts of the eye that can be affected are-

Tear film: which leads to dry eye syndrome

Sclera: Inflammation of the collagenous coats of the eye (sclera and cornea) is a serious complication of rheumatoid arthritis. Among these, scleritis is the most common. It may be classified as diffuse, nodular, necrotising (with or without inflammation [scleromalacia perforans]), and posterior. Necrotising scleritis without inflammation typically occurs in women of long standing rheumatoid arthritis and is typically bilateral. It begins as an asymptomatic yellow necrotic scleral patch in the uninflamed sclera. Progressive exposure of underlying uvea occurs as a result of scleral thinning, followed by staphyloma formation.

Episcleritis may be classified as nodular or diffuse, although the course is the same in both cases. Scleritis and episcleritis occur in approximately 4 to 10% of all

rheumatoid arthritis patients. Secondary intraocular inflammation including uveitis and serous retinal detachment frequently occur with severe scleritis.[14]

Cornea: Corneal changes may be found adjacent to areas of scleral inflammation or independently, in the absence of scleral changes. Localized infiltration of the cornea followed by development of epithelial defects and frank loss of cornea may occur.[14]

One of the following four types of keratitis may be seen:[15]

Sclerosing keratitis- Characterized by gradual thickening and opacification of the corneal stroma adjacent to a site of scleritis.

Peripheral corneal thinning (contact lens cornea)- Characterized by gradual resorption of peripheral stroma, leaving the epithelium intact.

Acute stromal necrosis- Diffuse peripheral scarring and vascularisation and occasionally epithelial breakdown and stromal melting.

Acute corneal melting.

Uvea: Anterior uveitis may occur.

Lens:[16] Posterior subcapsular cataracts have been reported, but these have been attributed to the long term steroid treatment that these patients receive rather than the disease process itself.

Retina, Choroid,Optic nerve: Secondary retinal detachment, choroiditis, optic neuritis and bilateral choroidal nodules have been reported.[17]

However, dry eye is by far the most common ocular manifestation in rheumatoid arthritis with a prevalence of nearly 20-50%. [18-20]

Immunopathogenic mechanisms responsible for dry eye:

It has been proved that there is T cell infiltration into various tissues in rheumatoid arthritis. Cytokines released by the infiltrating $CD4^+$ T cells are capable of altering conjunctival epithelial homeostasis. IL-17 alone or in conjunction with interferon (IFN)-[gamma] or TNF-[alpha] has been found to stimulate the production of inflammatory mediators such as IL-6, IL-8, granulocyte colony-stimulating factor, interferon-inducible protein (IP)-10, intercellular adhesion molecule-1, human leukocyte antigen-DR, and [beta]-defensin-2 by mucosal epithelial cells. IFN-[gamma] decreases goblet cell differentiation and increases expression of cornified envelope precursor proteins such as involucrin and small proline-rich protein-2. [21] There is also a relationship between T-cell infiltration of the conjunctiva and loss of goblet cells.

Approximately 10 to 15% of patients with rheumatoid arthritis, mostly women develop Sjogren's syndrome, a chronic inflammatory disorder characterized by lymphocytic infiltration of lacrimal and salivary glands. This leads to impaired secretion of saliva and tears and results in the sicca complex: dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca).

However, dry eye can occur even in the absence of features of Sjogrens syndrome. Patients having Sjogren's syndrome along with rheumatoid arthritis and those having only rheumatoid arthritis with no features of Sjogren's syndrome, both have been found to have increased HLA Dw3, HLA Bw44 and HLA DRw4. Increased amounts of IgA, IgM and IgG containing immune complexes are also

found in both these groups, suggesting that similar autoimmune mechanisms may be responsible for the ocular manifestations in both these groups of patients.[14]

Eye problems may be caused by associated conditions or medication side effects. Consequent visual impairment may increase the risk of general morbidity of the patient.

Studies have attempted to identify association of rheumatoid factor, rheumatoid arthritis activity and duration of rheumatoid arthritis with ocular manifestations in general and dry eye in particular.[22-24] While there are some reports supporting the evidence that dry eye is indeed associated with longer duration of rheumatoid arthritis and ocular manifestations are in fact more often seen in people with higher titres of rheumatoid factor; dry eye has not been found to be associated with rheumatoid arthritis activity. Fugita et al state that dry eye should always be considered regardless of the RA activity, because the severity of dry eye is independent of RA activity.[23]

ASSESSMENT OF DRY EYE SYMPTOMS:

Symptoms form an important part of assessment of any disease process and dry eye is no exception. Surveys on population based prevalence of dry eye have shown that symptoms are present in 25-35% of people.[25] However, studies have also shown a poor association between the signs and symptoms of dry eye.[26] The most common symptoms in patients of dry eye are, ocular fatigue, discomfort, grittiness, soreness, redness, foreign body sensation, light sensitivity, blurring of vision. These symptoms are found to occur in increased intensity as the day progresses. [27-29]

The National eye institute workshop on clinical trials in dry eye which gave a formal definition of dry eye concluded that all clinical trials concerning dry eye should include an assessment of subjective symptoms and functional life style through the use of a well designed and validated questionnaire and that such an instrument may be the best measure for determining the clinical efficacy of therapeutic interventions.

Numerous studies have been done to find the most common symptoms and to formulate a valid questionnaire.

The National Eye Institute visual function questionnaire (NEI VFQ – 25) is one such questionnaire to assess the symptoms of ocular disease. However, it surveys the general ocular health and is not reliable to capture the broad range of symptoms unique to a certain ocular disorder. [30]

Mc Monnies questionnaire, which is the patient perspective instrument specific for dry eye disease, has a formalized grading system and some published psychometric

properties. It primarily uses dichotomous responses (yes or no) to assess the presence of symptoms. [31] However, it was evaluated as a screening test to discriminate subjects with dry eye from normal population and not as an instrument to grade either dry eye symptom severity or its affect on vision related function.

A self administered *dry eye questionnaire* (DEQ) was tested on a sample of 1054 patients in Ohio, USA. The frequency of individual symptoms was tested in contact lens and non contact lens wearers which found that nearly 47% of the patients diagnosed with dry eye had symptoms so severe that they had to stop their daily activities and close their eye more than once a week.[32]

However, none of these studies had assessed the severity of symptoms of dry eye but tested only if symptoms were present or absent. In order to overcome this drawback, the OSDI questionnaire was designed.

The ocular surface disease index questionnaire (OSDI), is a 12 item questionnaire designed to provide a rapid assessment of symptoms of ocular irritation consistent with dry eye disease and their impact on vision related functioning. The questions were generated based on patient comments from several years of clinical studies. Each symptom is given an individual score and the final calculation takes into account the number of questions answered and the cumulative score. The reliability and validity of this questionnaire has been tested in a sample of 109 dry eye patients where it has been found to have excellent test-retest reliability and validity, effectively discriminating between normal, mild to moderate, and severe dry eye disease as defined by both the physician's assessment of severity and a composite disease severity score.[33] Like it has been with other trials , OSDI too has shown to

have moderate co relation with clinical signs among patients with dry eye disease who have tear deficiency. .But, it has demonstrated good sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease.

Due to these reasons, this questionnaire has been employed in the present study.

SIGNS OF DRY EYE:

The physical findings which may be seen are- filaments, meniscus floaters, mucus strands & papillary conjunctivitis. [34]

1) Filaments: When the cornea dries to a point that is incompatible with a healthy epithelial layer, some surface cells become dessicated and are shed, creating a small pit on the corneal surface. Lipid containing mucin will become attached to these pits; surface epithelium grows on these mucus cores and filament is formed.

2) Meniscus floaters: Arise from dead epithelial cells and fibrils of lipid contaminated mucin.

3) Mucus strands: These are strings of lipid contaminated mucus that have rolled up and been pushed into the cul de sac by shearing action of lids. These are more common in mucin deficient dry eyes.

At the cellular level: Morphological changes occur in the epithelial cells. There may be cohesion of cells, nucleo cytoplasmic ratios differ and keratinisation occurs. The changes occurring are graded based on the staining characteristics, shape of the cells, size of the nuclei and presence or absence of goblet cells.[35]

Grade 0: Epithelial cells are small and round. Nucleus is large, basophilic; N: C ratio is 1:2. Goblet cells are abundant, plump and oval. PAS positive cytoplasm is present.

Grade 1: Epithelial cells are larger and more polygonal. Eosinophilic staining cytoplasm is present. Nuclei are smaller with N: C ratio being 1:3.Goblet cells are decreased in number but maintain their shape with intensely PAS positive cytoplasm.

Grade 2: Epithelial cells are large, polygonal, may be multinucleated. They have variably staining cytoplasm. Nuclei are small with N:C ratio of 1:4 to 1:5. Goblet cells are markedly decreased in number, smaller and less intensely positive. They have poorly defined cellular borders.

Grade 3: Epithelial cells are large, polygonal with basophilic staining cytoplasm. Nuclei are small, pyknotic or completely absent. N:C ratio is 1:6. Goblet cells are completely absent.

PSYCHOLOGICAL EFFECTS OF DRY EYE:

Dry eye syndrome is not a common cause of vision loss, but it is still a serious issue for people who have it. The symptoms become progressively troublesome and exert an increasing burden on the patients as the disease progresses or increases in severity. These types of patients have various degrees of health-related QoL impairment, can become frustrated with their treatment course, repeatedly visit doctors and specialists seeking treatment changes, and may seek alternative treatments leading to significant utilization of medical resources. Studies have shown that these patients are reported to have significant loss of productivity each year, often losing approximately 5 work days and working an average of 208 days with dry eye symptoms.[36]

It reduces the functional visual acuity of the patient and also leads to his life long dependence on his doctor. Sufferers of dry eye syndrome are more likely to report problems with daily activities, including reading, using a computer, driving and watching television, than people without dry eye syndrome.

The signs do not manifest till late stages of the disease. If not detected early, dry eye can lead to complications which are as follows:

COMPLICATIONS:[34]

1) Sterile stromal ulcers: The corneal melt which occurs is typically an oval, non infiltrated ulcer situated at or just below the visual axis with its longest dimension horizontal. The ulcers tend to progress quickly and often perforate.

2) Blepharitis and Conjunctivitis: There is increased incidence of infection due to loss of normal antibacterial tear substances, lysozyme, β lactam and lactoferrin.

3) Band keratopathy.

4) Keratinization.

5) Corneal vascularisation.

DIAGNOSTIC TESTS:

As the symptoms are non specific and signs do not manifest till late stages of the disease, objective assessment in the form of tests is of utmost importance in the evaluation of a suspected case of dry eye or in the screening for dry eye.

There are many suggested dry eye diagnostic test batteries in literature. But, there has been no systematic description of the standard of care in diagnosing dry eye. In a retrospective review of patients charts performed in 4 clinical settings with a sample size of 467 patients in USA, it was found that fluorescent staining was used maximally, followed by TBUT, tear meniscus, Schirmer and Rose bengal tests. It was also found that performance of 2 diagnostic test procedures, often including patients symptoms appeared to represent the current standard care in diagnosis of dry eye.[37]

Another study conducted in Massachusets showed that the most frequent first choice test preferred by Ophthalmologists was Schirmer test and its modifications (79%) followed by rose bengal staining(59%), TBUT (47%) and fluorescent staining(50%). Tear film evaporation, tear protein analysis, tear ferning and impression cytology were found to be the least used tests for diagnosis.[38]

The global workshop on clinical trials for dry eye suggests that diagnostic tests should include those which assess the interpalpebral surface damage, tear instability and tear hyperosmolarity. Among all the tests available, 4 tests given below assess precisely these criteriae. In addition, they are easy to perform on out patient basis and harmless to the patient.

Schirmer test:

This has been, for years, the most common means of measurement of tear production. The details of this test were first published in 1903. [9] It involves folding sterile filter paper strips and inserting them between the lower lid and the globe at lateral one third of lid margin. The test can be performed with or without topical anaesthesia or with nasal stimulation.

Much confusion and disagreement exists in literature as to the validity and usefulness of Schirmer test. Without anaesthesia the test is believed to measure reflex and basic tear secretion whereas with anaesthesia, it is believed to measure basic tear secretion devoid of reflex components. The false positive results appear to be reduced somewhat if the test is performed without local anaesthesia. Studies conducted in Philadelphia have posed a question mark over the existence of an entity called pure basic secretion and the validity of performing the test with anaesthesia because the use of anaesthesia reduces conjunctival, corneal and lid margin sensitivity but does not totally suppress reflex tearing. [39]

The Schirmer test (ST) is most commonly performed with the patient's eyes open and blinking normally, but some clinicians prefer performing it with the patient keeping his eyes closed. A study was done in Turkey, to compare the repeatability of the 2 STs. They found that, closing the eyes during ST results in less blinking and may help to maintain more stable and uniform conditions under which the test is performed. When the eyes are closed, role of the lid margins and eyelashes in stimulating tear secretion and the influence of external factors such as temperature, evaporation, and humidity are reduced. It is also easier for the patient to keep the eyes still because external visual stimulants are absent, and this reduction in eye movements minimizes irritation caused by the paper. This in turn reduces excess

reflex tearing, which is a major factor that compromises ST's reliability. There were statistically significantly higher readings with the eyes open,in this study supporting this increase in reflex tearing when the eyes are open during ST. [40]

Despite conflicting reports, Schirmers test still continues to be a widely used test for assessment of dry eye.

Tear film Break Up Time (TBUT):

TBUT was described by Norn and revised by Lemp and Holly.[41] It is a test which measures the tear film stability. The tears are stained with fluorescein dye and the time interval is measured between a complete blink and first appearance of a dry spot in the precorneal tear film. BUT can be measured invasively by using fluorescein (FBUT) or non-invasively using a keratometer or a xeroscope (NITBUT).

The steps involved in the break up of tear film as per Holly's (also known as Holly and Lemp's) mechanisms are as follows:

- The tear film thins uniformly by evaporation.
- When it is thinned out to some critical thickness, a significant number of lipid molecules begin to be attracted by the mucin layer and migrate down to this layer. This migration process is enhanced if there is any spontaneous local thinning.
- When the mucin layer on the endothelium is sufficiently contaminated by the lipid migrating down from the top surface of the tear film, the mucin becomes hydrophobic and the tear film ruptures.

Blinking then occurs to repair the rupture by removing the lipid contaminant from the mucin layer and restoring a thick aqueous layer.

The fluorescein tear break up time has been shown to be dependent on the reduction of surface tension by mucins. When the tear mucin is reduced, as reflected by a fall in conjunctival goblet cell density or a rise in surface tension, BUT is also reduced.

A study was done in 1983 in Aligarh to know the BUT in normal Indian subjects, as no major study had been undertaken before this in our part of the world. It was found that BUT was lower, less than 15 seconds when compared to westerners in whom it has been found to be 20 to 30 seconds normally. The lower rate was attributed to tropical climate conditions. [42]

Another study was done in Canada in 2005, where the tear break up dynamics were videotaped in order to study the phenomenon of tear break up in dry eye and control subjects and its impact on dry eye symptoms. This study clearly demonstrated that the tear break up is more rapid and extensive among dry eye subjects compared with controls. Even after the first break, tear film of many dry eye subjects continued to disrupt over larger areas of cornea. This study has further reinforced the need for using TBUT for evaluation of dry eye. [43]

While performing the procedure, it is common clinical practice to take several tear breakup time measurements and average the results. Nichols KK and co workers found that averaging the two readings resulted in improved repeatability. [44] Therefore, taking two measurements and averaging yields a longer and more

repeatable tear break-up time and may be a more appropriate technique for clinical practice and clinical studies.

Rose Bengal staining:

Rose Bengal is a vital dye that stains altered corneal and conjunctival epithelium. Rose Bengal staining ensues whenever there is poor protection of surface epithelium by the pre ocular tear film. In addition, it has a phototoxic effect which causes ocular irritation after instillation. [45]

The precise change in the epithelial cell membrane that permits dye uptake is still unknown. As early as 1933 Sjogren used the rose bengal stain for the diagnosis of keratoconjunctivitis sicca (KCS). Rose Bengal is a fluorescein derivative, i.e. tetrachloro tetraiodo fluorescein sodium. Despite their clinical similarity, the two dyes differ completely with regard to their staining properties. Fluorescein does not stain cells or tissues but diffuses into the intercellular spaces from a surface defect. Rose Bengal on the other hand, has the characteristic to stain surface cells of the cornea and conjunctiva that tend to keratinize.

Van Bijsterveld (1969) introduced numerical scoring for the intensity of staining with rose Bengal of both medial and lateral bulbar conjunctiva and of the cornea.[46] Each section was given a score of up to three points, so that a maximum score of nine could be obtained. He found the best staining intensity score limit to differentiate between normal persons and patients with keratoconjunctivitis sicca to be 4. In his comparative study, Van Bijsterveld found that, with a score limit of 4, the combination of results of the Schirmer test and rose bengal test was no better than the

results of rose bengal test alone. At the stated limit, he found the probability of misclassification to be around 5%.

It has been recommended as one of the tests which can assess ocular surface damage in dry eye.

Conjunctival Impression Cytology:

Believed to be one of the best methods for study of conjunctival or ocular surface, conjunctival impression cytology by means of cellulose acetate strips was first introduced by Egbert and associates in 1977 as a minimally invasive conjunctival biopsy.[47]

It refers to the application of a cellulose acetate filter to the ocular surface to remove the superficial layers of ocular surface epithelium. These cells can then be subjected to histological, immunohistological or molecular analysis. Generally, 2 to 3 layers of cells are removed in one application but deeper cells can be accessed by repeat application over the same site. It is non invasive, relatively easy to perform and yields reliable information about the area to be sampled. [48]

Before the introduction of this method, study of conjunctival surface was attempted using excised pieces of tissue or by scraping the conjunctival epithelium. They experimented with a variety of methods including cellophane tape, photographic film, various synthetic filters and found that original Millipore filters were best for this purpose. It was introduced mainly to study the goblet cell density of the ocular surface in the initial period after introduction.

In the later years, the method gained popularity and became a standard method for study of ocular surface in various conditions such as viral keratoconjunctivitis, [49] keratoconjunctivitis sicca, vitamin A deficiency (where it can pick up mild xerophthalmia),[50] changes occurring in conjunctival epithelium in chronic renal failure (where the conjunctival epithelial features in chronic renal failure patients with or without calcium deposits have been studied),[51] surface changes which may occur in psoriasis, [52] ocular surface malignancies [53] etc.

However, the widest application of this investigation has been in the field of dry eye syndrome. As early as 1991, Reddy M and associates did a comparative study of conjunctival biopsy versus impression cytology to study the histopathological changes occurring in conjunctiva in dry eye states and found that impression cytology was as effective as biopsy for diagnostic purposes. [54] It helps establish not only if dry eye is present or not but also aids in grading the severity of dry eye.

Using this technique, studies have been done, not only in the field of detection of the disease process but also in looking for reversal of changes which may occur after use of topical medication.

The process has undergone tremendous improvement since the time it was introduced. Initially, the extent of modification was limited to the variation of chemicals used for processing the strips. But, in the later years, a transfer technique was introduced where the cellulose acetate impression was directly transferred to the slide which eliminated the need for processing of strips. A study done in Mumbai found that the technique was extremely useful to visualize the state of superficial conjunctival cells, is easy to perform and the time taken for the entire procedure from

taking impression to seeing the slide does not take more than 8-10 minutes. The relationship of various cells to each other is also maintained.[55]

A recent study has shown that nylon paper can also be used as an alternative to cellulose acetate filter paper for conjunctival impression cytology, with comparable results.[56]

A number of recent advances have improved the ability to measure dry eye clinical signs and symptoms. Standard grading scales have been developed with which ocular surface stains are assessed in various conditions. Tear film instability can be dynamically monitored through image analysis of fluorescein videography, corneal topography, interferometric imaging and optical coherence tomography, and wavefront technology, which allows real-time tracking of vision during periods of tear instability.

It has been proved that dry eye syndrome can cause severe consequences if not detected early in the course of the disease. It is also true that the occurrence of this condition is higher with certain systemic conditions, the most common one being rheumatoid arthritis. Hence, the study of prevalence of dry eye by means of tests and its possible relationship with rheumatoid factor is highly relevant.

METHODOLOGY

The study titled "A ONE YEAR CROSS SECTIONAL STUDY OF DRY EYE IN RHEUMATOID ARTHRITIS PATIENTS" was conducted in the Department of Ophthalmology at KLES Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

STUDY:

The study was conducted on 70 patients who had been diagnosed to have rheumatoid arthritis at the immunology clinic of the hospital using pre determined guidelines. It was a one year cross sectional study with the study period ranging from January 2007 to January 2008. The sample size of 70 was arrived at based on previous statistics of patient input.

Written informed consent was taken before enrolling the patients in the study. An OSDI questionnaire was administered to all participants to assess the symptoms of dry eye and correlate them with the signs.

A complete slit lamp examination was conducted on the patients to identify objective signs, specifically looking for conjunctival congestion, increased conjunctival folds, xerosis, corneal dryness (assessed by the loss of corneal sheen and distorted reflex on torch light examination) and features of other ocular complications of rheumatoid arthritis.

Following this, four diagnostic tests were done, based on which the diagnosis of dry eye was made. Participants were labelled as having dry eye if at least two out of these four diagnostic tests were positive. This criteria of two tests to diagnose dry

eye was adopted in order to increase the detection rate of dry eye and hence arrive at an accurate prevalence.

INCLUSION CRITERIA:

1) Patients diagnosed to have rheumatoid arthritis according to American College of Rheumatology (ACR) criteria for diagnosis & classification of rheumatoid arthritis (revised in 1987), with or without symptoms of dry eye.

2) Age group ranged from 16-65 years, since patients aged less than 16 come under the category of juvenile rheumatoid arthritis and the age of > 65 years itself is an independent risk factor for occurrence of dry eye.

EXCLUSION CRITERIA:

1) Age group < 16 years and > 65 years.[57,58]

2) Patients suffering from diabetes mellitus and thyroid disease.[59,60]

3) Contact lens users.[61]

4) Patients who had undergone cataract or refractive surgery.[62]

5) Patients on xerogenic drugs.

These patient groups were excluded from the study because all these form independent risk factors for the occurrence of dry eye, which would have led to bias in the study. After exclusion of all patients with these characteristics, the total study sample of 136 eyes of 70 patients was obtained. 4 patients had undergone cataract surgery in one of the eyes. That eye was excluded and the other eye was considered for the study.

INVESTIGATIONS PERFORMED:

1) **Schirmer test:** This test was performed before the other tests as it had to be done before instillation of anaesthesia.

Procedure:

It was carried out using 5 X 35 mm sterile strips of Whatman No.41 paper. Patient was made to sit in relatively dark area in a room with fan switched off. The terminal rounded end of the strip was folded at the pre marked area along 90^{o} angle. Touching the paper strip directly with the finger was avoided in order to avoid contamination of skin oils. The patient was then asked to look up, lower lid retracted and the test paper inserted in the lower cul de sac at the junction of medial $2/3^{rd}$ and lateral $1/3^{rd}$ of the lid. Adequate care was taken during the procedure to ensure that the paper did not touch cornea, in order to avoid reflex tearing. The patient was asked to keep eye closed for 5 min to avoid loss of tear film by evaporation and to avoid reflex tear secretion which may be brought about by blinking.[40] Then the amount of wetting was measured from the fold till the wetted strip area, in mm. The procedure was performed without instilling anaesthesia.

Interpretation: Measurements of < 10 mm were considered to be positive. Readings >/= 10 mm were considered as negative.[8]

2) **Tear film break up time (TBUT) :** The TBUT is the time in seconds between the last blink and the appearance of the dry spot.

Procedure:

The patient was seated at the slit lamp. A drop of antibiotic solution was placed on a sterile fluorescein strip. This drop mixed with fluorescein was allowed to fall into the lower cul de sac of the eye. Subject was asked to close the eye for few seconds, blink several times and move her eyes around to thoroughly mix the fluorescein with the tear film and to allow even distribution of dye. Then, he/ she was asked to look straight ahead without blinking. The tear film over the lateral half of cornea was then examined with a broad beam and cobalt blue filter, watching for an area of tear film rupture manifested by a black island within the green sea of fluorescein. The time elapsed between the last blink and appearance of first black spot was termed as tear film break up time and noted in seconds. This kind of measurement was taken for three successive blinks and the mean of this was noted as the final reading.

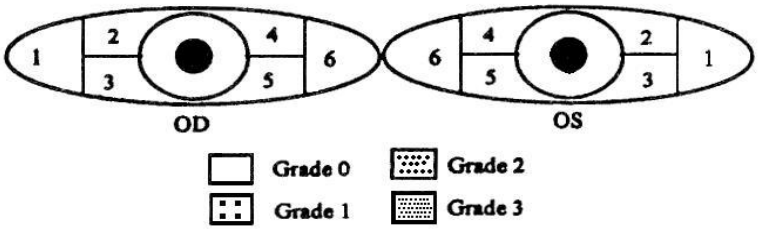
Interpretation: Break up time of less than 10 seconds was considered as positive, indicative of dry eye. Greater than or equal to 10 seconds was considered negative.[8]

3) Rose Bengal test: It is a means of assessing ocular surface damage using the rose bengal dye.

Procedure:

One drop of antibiotic solution was put on a sterile, commercially available rose bengal strip. This drop was allowed to roll into the lower cul de sac of each eye. After 15 seconds, the eye was examined for staining of cornea and conjunctiva.

The amount of staining in 6 areas of eye was then recorded and graded based on modified Von Bijsterveld rose bengal grading map. A quantitative scale of 0 to 3 was used in each area of the conjunctiva of each eye. A summation of the points assigned to each area was made for each eye.



Interpretation: An additive score of total 4 or more in the eye constituted a positive test. Less than this value was considered as a negative test. [9]

4) Conjunctival Impression Cytology: This is a fool proof method of assessing the ocular surface damage.

Procedure:

This test was conducted using cellulose acetate strips having a pore diameter of 28 microns. The strips were initially stored in a solution of 30% methanol. Just

before the test, they were placed in normal saline to remove traces of methanol. Then, they were cut to a size of 3 × 10 mm. Proparacain was instilled into the eye. Patient was asked to look towards the nasal side. The strip was then placed on the temporal bulbar conjunctiva using forceps. Gentle pressure was applied using a glass rod with rounded end for 8-10 seconds. Paper was removed using peeling motion and immediately placed on glass slide. The imprint was transferred to the slide by gently rolling the glass rod on it. The slide was placed in a solution containing 95% ethanol (fixative) , till further staining.

4 such impressions were taken for each patient, two for each eye. The slides were labeled as A,B,C,D, with A and B belonging to right eye and C and D belonging to left eye. Slides A and C were stained using PAS stain. Slides B and D were stained using H and E stain. The slides were interpreted using the grading system described by Nelson.

Interpretation: The eyes having grade 2 or grade 3 changes were considered positive for dry eye. Eyes with grade 0 or grade 1 change were considered negative.[35]

Staining technique:

***H and E staining*[63]**

Procedure

- Deparaffinise with xylene – 5 -10 minutes.
- Absolute ethyl alcohol- 5 minutes.
- 95% ethyl alocohol – 5 minutes.
- Wash with tap water.

- Harris hematoxylin -10-15 minutes.
- Differentiated with 1% hydrochloric acid.
- Wash in running tap water.
- Bluing with running tap water.
- Stain with watery eosin -15 seconds.
- Rinse in 80% to 90% alcohol – 2 changes.
- Rinse in absolute alcohol – 2 changes.
- Clear in xylene.
- Mount with DPX.

Results

Nuclei – Blue to blue black.

Cytoplasm and other substances – Pink.

Periodic Acid Schiff. [63]

Principle

Substances containing vicinal glycol groups or their amino/alkyl amino derivatives are oxidised by periodic acid to form dialdehydes, which combine with Schiff reagent to form an insoluble magenta compound. This stain therefore demonstrates glycogen and neutral mucosubstances.

Staining procedure

- Dewax the section.
- Bring to water.
- Oxidize with 1% aqueous periodic acid for 5-10 minutes.
- Wash well with several changes in distilled water.
- Cover with Schiff reagents for 10-30 minutes.
- Rinse for 2 minutes in freshly prepared sulphite.
- Wash in running tap water for 5-10 minutes.
- Wash in water.
- Rinse in absolute alcohol.
- Clear in xylene and mount with DPX.

Results

PAS positive substances –Magenta pink.

Nuclei –Blue.

RESULTS

Table 1: Characteristics of the study population

Characteristics	Number
Total number of patients of rheumatoid arthritis	70 (136 eyes)
Age group	21-65 years
RA factor positive	24 patients
Schirmer test positive	56 eyes
Tear film break up time positive	26 eyes
Rose Bengal test positive	51 eyes
Impression cytology positive	50 eyes
Dry eye present(2 or more tests positive)	34 patients(56 eyes)
Dry eye absent	36 patients(80 eyes)

The total number of patients examined in our study was 70. The eyes included in the study were 136. The age group was between 21 to 65 years, with the mean age of the patients being 47.92 years. They were recruited irrespective of their sex. Of the total number of patients, 57 were females and 13 were males with a female to male ratio of 4.38:1. Among the entire group, 34 patients (56 eyes) were diagnosed to have dry eye based on the tests.

Table 2: Dry eye in relation to Age distribution

Age (years)	Dry eye present No. of patients (%)	Dry eye absent No. of patients (%)	Total No. of patients (%)
21-30	0	5 (100%)	5
31-40	6 (31.5%)	13 (68.42%)	19
41-50	8 (53.53%)	7 (46.66%)	15
51-60	12 (60%)	8 (40%)	20
61-70	8 (72.72%)	3 (27.27%)	11
Total	34	36	70

$\chi 2$- 9.089 p= 0.028 (S)

The entire study population was divided decade wise into subgroups and the relationship of age with dry eye prevalence was studied. The youngest patient was of 21 years and the oldest was 65 years. Mean age was 47.96±11.55 years.

Graph 1: Distribution of patients according to age

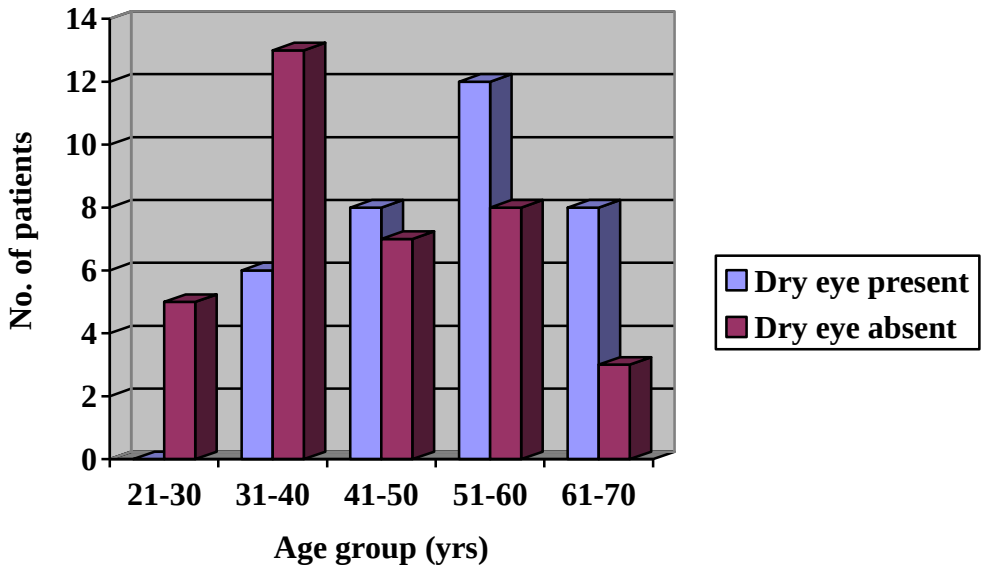


Table – 3: Dry eye in relation to sex distribution

Sex	Dry eye		Total
	Present	Absent	
Females	29	28	57
Males	5	8	13
Total	**34**	**36**	**70**

χ2- 0.653 p= 0.419

There were 57 females and 13 males in the study group with the female to male ratio being 4.38:1

Graph 2: Distribution of dry eye according to gender (percentage)

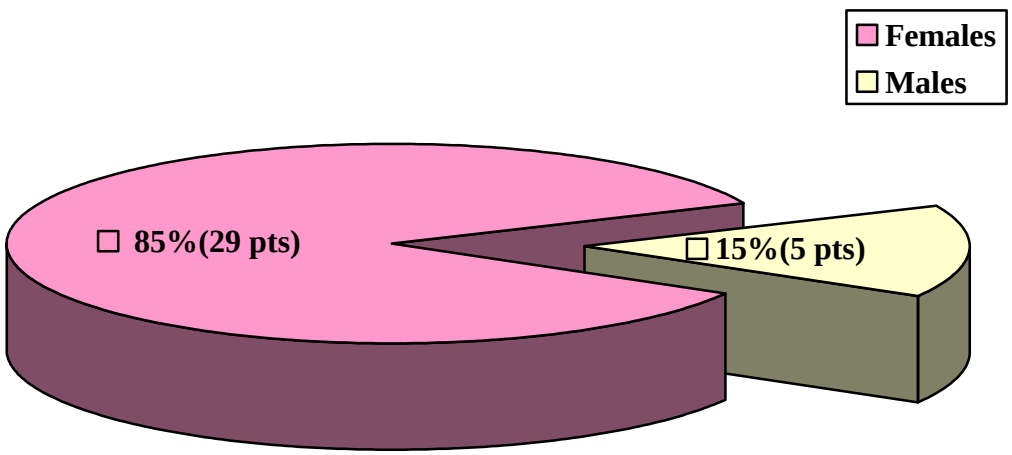


Table – 4: OSDI Scores

OSDI	No. of Patients
0	6
1-33	45
34-66	12
67-100	6
Total	**70**

The ocular surface disease index (OSDI) was administered to the patients before subjecting them to examination or tests. Of the entire study group, 27.1% responded with symptoms of moderate to severe dry eye.

Graph 3: Distribution of patients according to OSDI scores

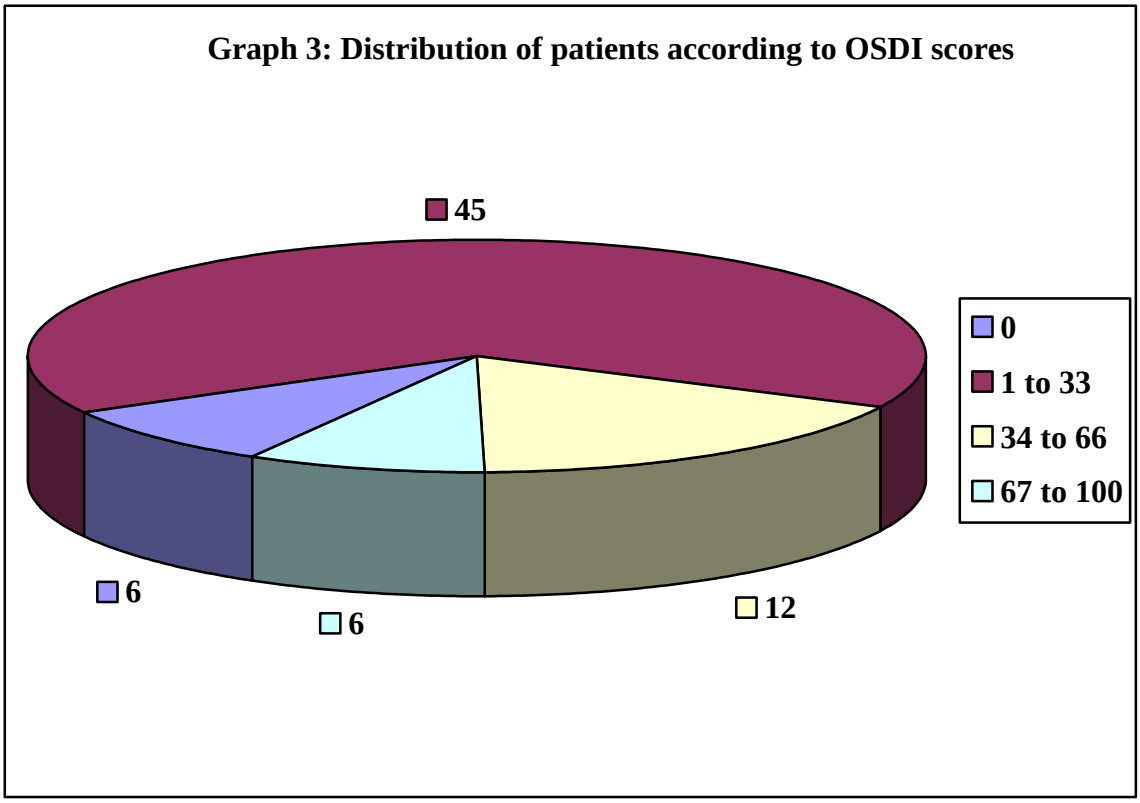


Table – 5: OSDI scores and correlation with dry eye

OSDI scores	Dry Eye		Total No. of eyes
	Present	Absent	
0	0	12	12
1-33	39	50	89
34-66	7	16	23
67-100	10	2	12
Total	**56**	**80**	**136**

χ2- 10.174 p=0.006 (S)

The eyes of the patients showing positive symptoms were then analysed and the symptoms were compared with the signs to look for correlation between symptoms and signs.

Graph 4: OSDI scores and their correlation with dry eye

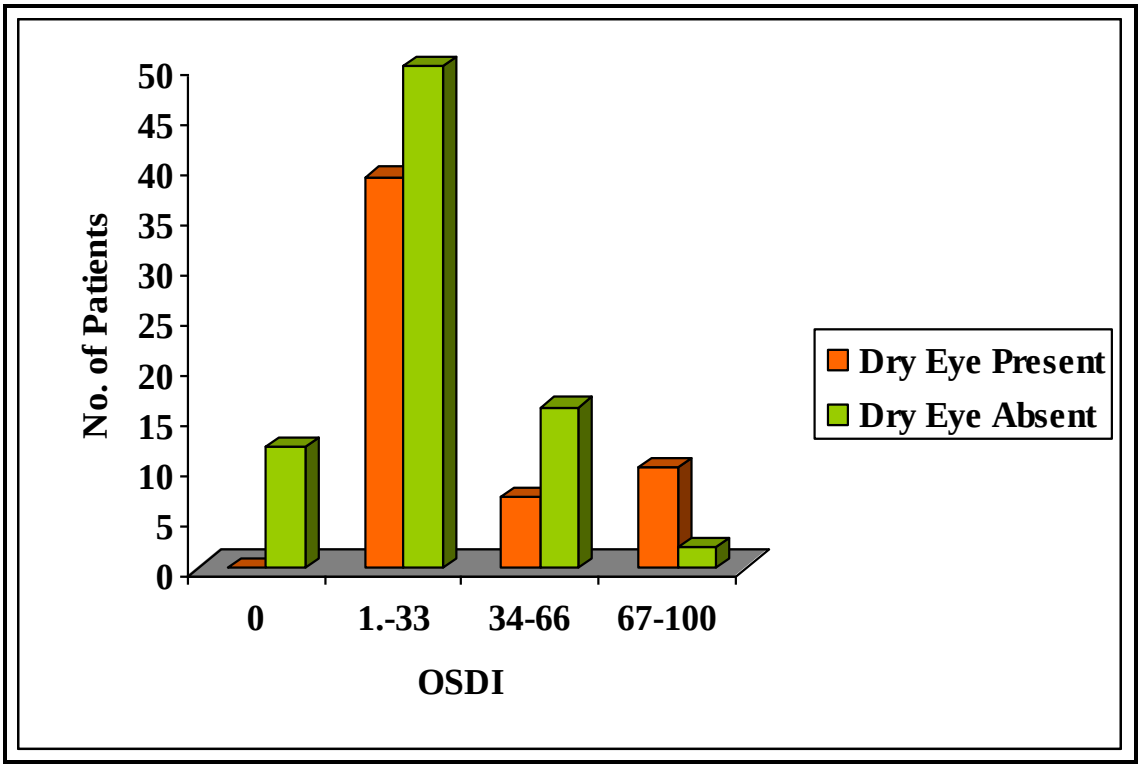


Table 6: Relationship between duration of rheumatoid arthritis and dry eye

Duration of RA (years)	Dry eye present (No. of patients)	Dry eye absent (No. of patients)	Total
0-4	20	23	43
5-9	10	8	18
10-14	2	4	6
15-19	2	1	3
Total	34	36	70

$\chi 2 = 0.485$ $p=0.784$ (NS)

The duration of rheumatoid arthritis in the patients was divided into 5 years interval in order to look for any relationship between duration of the disease and dry eye. The minimum duration of rheumatoid arthritis was 1 month and maximum was 19 years. Mean duration of RA was 4.51 years.

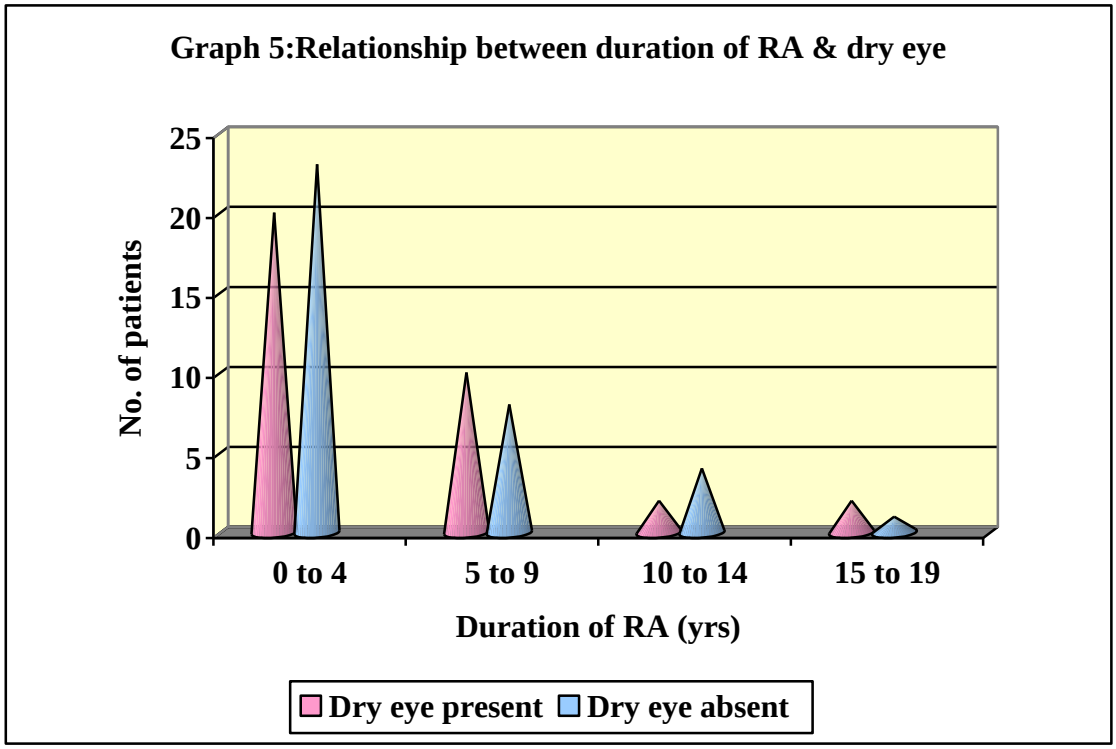


Table – 7: Relationship of RA factor & dry eye

RA factor	Dry eye		Total
	Present	Absent	
Positive	12	12	24
Negative	22	24	46
Total	**34**	**36**	**70**

χ2- 1.303 p=0.253

24 people (34.28%) tested positive for rheumatoid factor in the study group. Among those who tested positive, 12 patients (50%) showed evidence of dry eye. Among those who tested negative for rheumatoid factor, 22 patients (47.8%) showed evidence of dry eye.

Table 8: Relationship between RF titres & dry eye

RF titres	Dry eye present	Dry eye absent	Total
20-80	2	2	4
160-250	6	4	10
$\geq$ 320	4	6	10

The RF titres among patients in our study were between 20 (lowest positive) and 320 (highest positive). The titres were divided into three groups for the purpose of comparison.

Table – 9: Presence of dry mouth

Dry mouth	Dry Eye		Total
	Present	**Absent**	
Present	12	5	17
Absent	22	31	53
Total	**34**	**36**	**70**

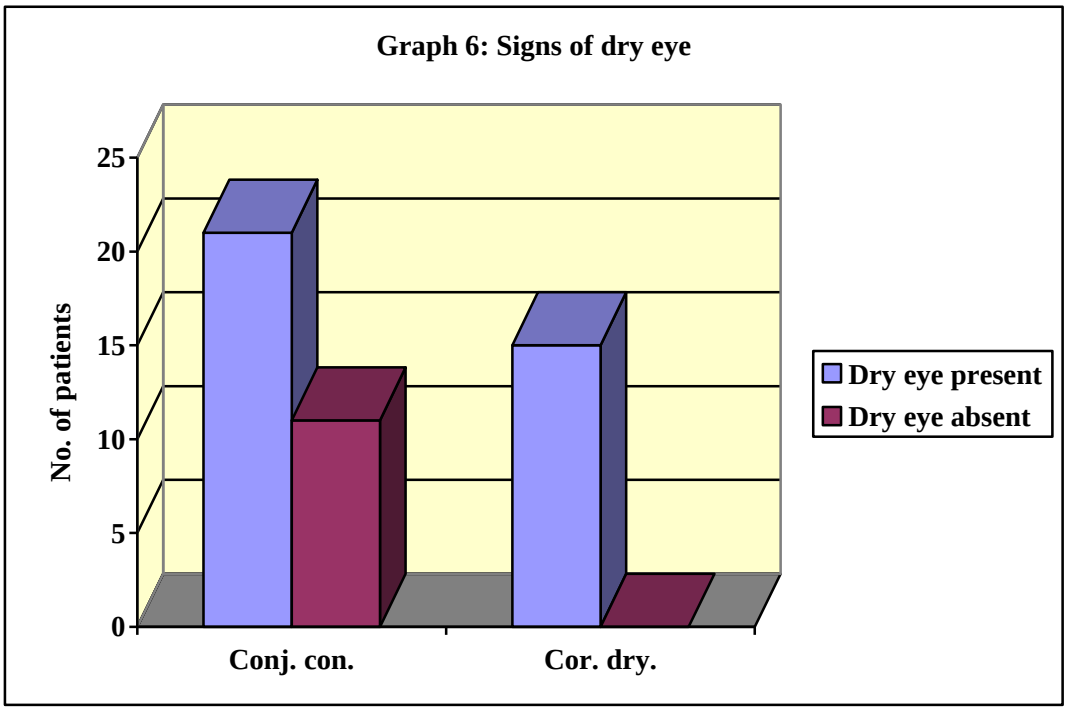
The patients were asked for history of dry mouth during recruitment into the study. This data was used to assess the number of people presenting with both dry mouth and dry eye. 12 patients (17.14%) were found to have evidence of both dry mouth and dry eye. 5 patients (7.1%) had a history of dry mouth but no evidence of dry eye.

Table – 10: Signs of dry eye

Signs	Dry Eye		Total
	Present	Absent	
Conjunctival congestion	21	11	32
Corneal dryness	15	0	15

χ2- 10.327 p=0.001 (VS)

A total of 32 eyes showed evidence of conjunctival congestion in the interpalpebral area, among which 21 (65.6%) eyes showed evidence of dry eye also when the tests were performed. Similarly, corneal dryness was noted in 15 eyes and in all these eyes, dry eye was proved by means of objective tests. Other signs present were, corneal vascularisation (4 eyes) and corneal opacity (1 eye). Scleral thinning was noticed in 4 eyes.



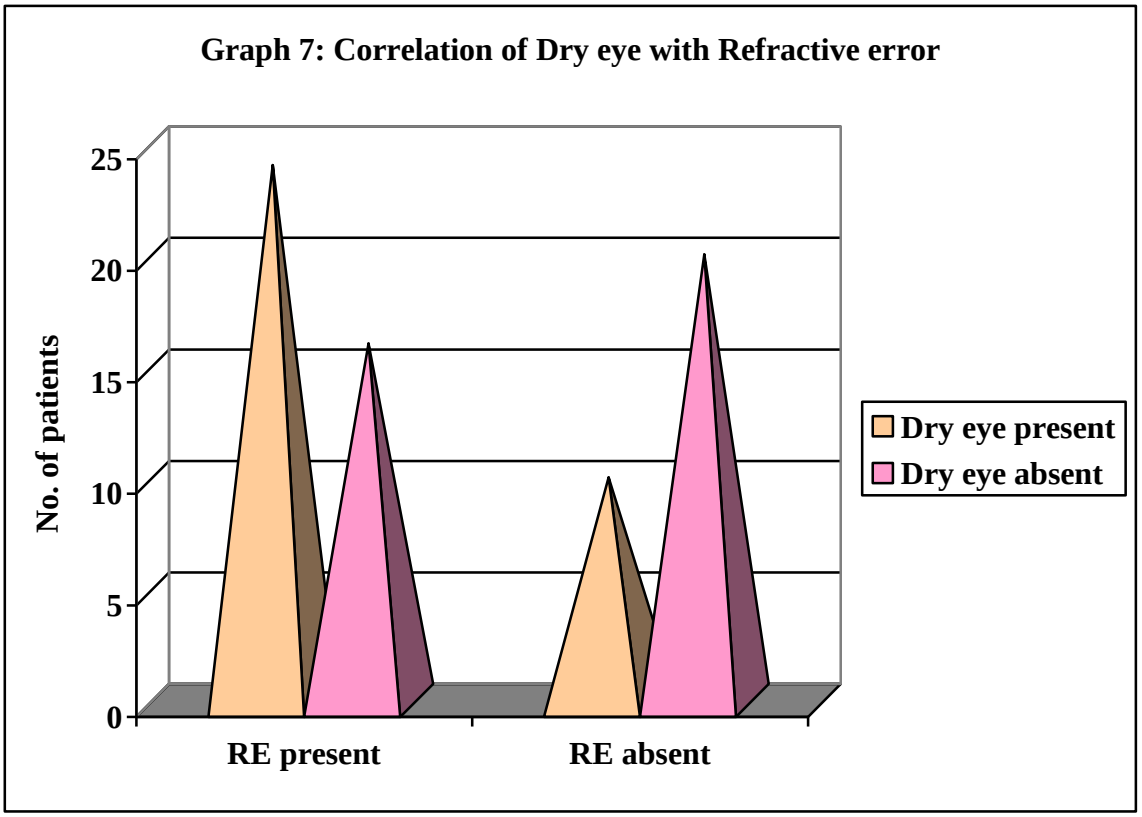
Key : Conj. con.- Conjunctival congestion; Cor. dry- Corneal dryness.

Table – 11 : Relationship between refractive error & dry eye

Refractive error	Dry Eye		Total
	Present	Absent	
Present	24	16	40
Absent	10	20	30
Total	**34**	**36**	**70**

χ2- 4.880 p= 0.027 (S)

40 patients (57.14%) among the total study population, had some form of refractive error and a history of use of spectacles. Among these, 24 patients (60%) had evidence of dry eye.



Key: RE- Refractive error.

Table 12: Results of Schirmer test

Schirmer test	Dry Eye		Total
	Present	Absent	
Positive	51	5	**56**
Negative	5	75	**80**
Total	**56**	**80**	**136**

A total of 56 (41.17%) eyes gave a wetting of less than 10 mm on performing the Schirmer test. Among these, 51 were proved to be positive for dry eye based on pre determined diagnostic criteria. The Schirmer test showed a sensitivity of 91.1% and specificity of 93.7%. The positive predictive value of the test was found to be 91.07% and the negative predictive value was 93.7%.

Table 13: Distribution of patients according to Schirmer test results.

Schirmers (mm)	0-5	6-10	>10	Total
No. of patients	20	11	39	70
% of patients	28.6	15.7	55.7	100

Among the 31 patients who gave a positive result for dry eye based on the Schirmer test in one or both eyes, 20 patients (28.6%) had a wetting of less than or equal to 5 mm. The rest i.e. 11 patients (15.7%) had a wetting of between 6 to 10 mm in one or both eyes, which is indicative of mild to moderate dry eye.

Table 14: Results of tear film break up time (TBUT) test

TBUT	Dry Eye		Total
	Present	Absent	
Positive	26	0	26
Negative	30	80	110
Total	**56**	**80**	**136**

TBUT was the second test to be performed. It was found to be positive (< 10 seconds) in 26 eyes (19.11%). All the eyes which gave a positive result showed objective evidence of dry eye. This test was found to have a sensitivity of 46.4% and specificity of 100%. Its positive predictive value was 100% and negative predictive value was 72.7%.

Table 15: Results of Rose Bengal test

Rose Bengal Test	Dry Eye		Total
	Present	Absent	
Positive	48	3	51
Negative	8	77	85
Total	56	80	136

A total of 51 eyes (37.5%), showed positive staining. Among these, 48 eyes (94.1%) were positive for dry eye. The test was found to have a sensitivity of 85.7% and specificity of 96.2%. The positive predictive value of the test was 94.1% and negative predictive value was 90.6%.

Table 16: Results of Impression cytology

Surface changes	Dry Eye		Total
	Present	Absent	
Present	44	6	50
Absent	12	74	86
Total	**56**	**80**	**136**

The histopathological changes occurring on the conjunctival surface due to dry eye were studied using this test. 50 eyes (36.76%) showed grade 2 or grade 3 changes, according to Nelson grading system. Among these, 44 eyes were proved to be having dry eye based on the diagnostic criteria set earlier. The test had a moderate sensitivity of 78.5%, specificity of 92.5%, positive predictive value of 88% and a negative predictive value of 86%.

Table 17: Comparison of screening procedures for dry eye

Procedure	Sensitivity	Specificity	+ve predictive value	-ve predictive value
Schirmer test	91.1	93.7	91.1	93.7
TBUT	46.4	100	100	72.7
RB test	85.7	96.2	94.1	90.6
CIC	78.5	92.5	88	86

Key:

TBUT: Tear film break up time

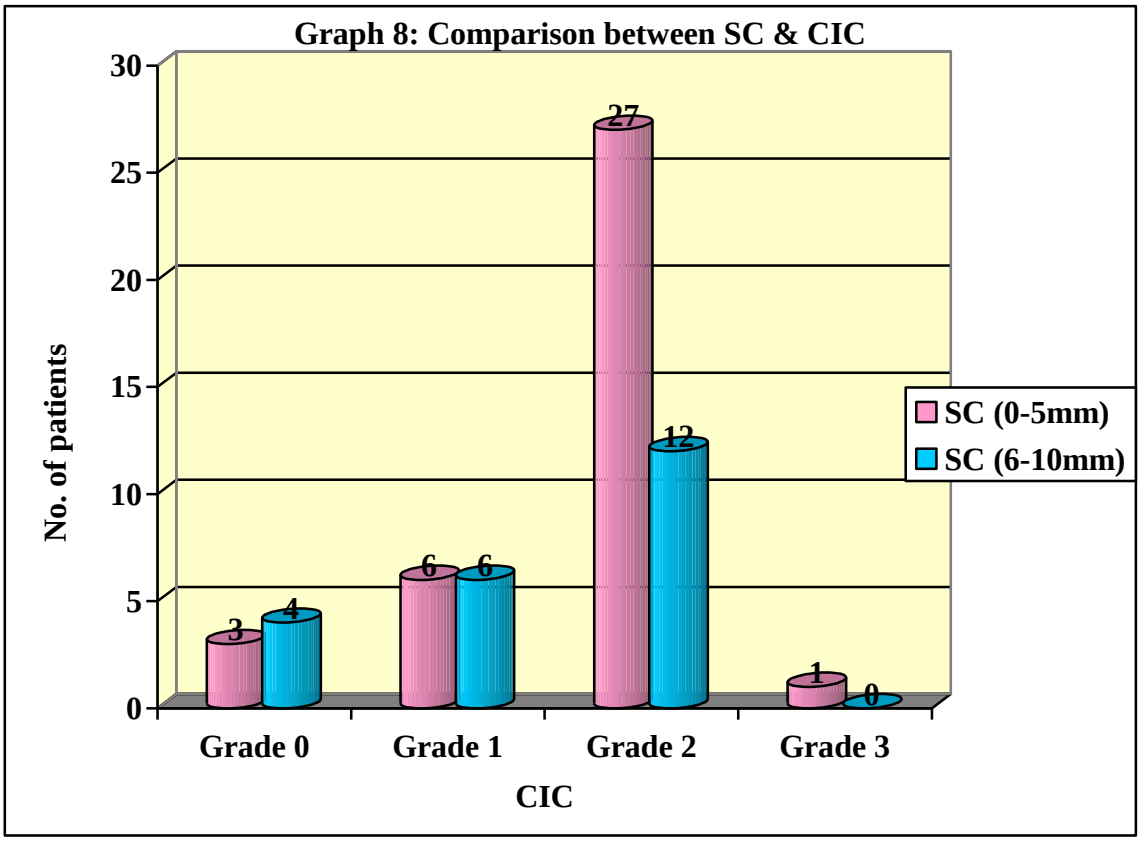
RB test: Rose Bengal staining

CIC: Conjunctival impression cytology

Table 18 : Association between Schirmer score and impression cytology

CIC grade	Schirmer score (0-5mm)	Schirmer score (6-10mm)	Total
Grade 0, 1	9	10	19
Grade 2,3	28	12	40
Total no. of eyes	37	22	59

χ2- 1.937 p= 0.1640 (NS)



Key:

SC- Schirmer score

CIC- Conjunctival impression cytology

DISCUSSION

Rheumatoid arthritis is the most common rheumatic disorder with a prevalence of as high as 1% in general population. The pathogenic mechanisms underlying this disease have been widely studied. It has wide extra articular manifestations with ocular manifestations being as high as 39%.

Prevalence of dry eye

Dry eye forms a major chunk of ocular manifestations and due to its frequent under diagnosis, can lead to potentially vision threatening complications. Determining the prevalence of dry eye in rheumatoid arthritis was the primary objective of our study. Among the total sample of 70 patients, we found 34 patients to have evidence of dry eye either in one or both eyes, based on the positive results of atleast two out of four objective tests. The prevalence of dry eye was 48.5% (Table 1).

Table 19: Comparison with other studies

Studies	Year	Prevalence of dry eye
Chandigarh study [17]	1977	29%
Yugoslavia study [64]	1997	45%
Norway study [65]	1999	29%
Japan study [23]	2005	47%
Mumbai study [66]	2006	27.3%
Czech study [24]	2007	74%
Our study	**2008**	**48.5%**

The previous studies done on Indian population have shown a relatively lower prevalence of dry eye compared to similar studies done on western population. However, our study noted a prevalence of 48.5% among the tested rheumatoid arthritis patients which correspond to the observations of Zlatano et al.[64] Punjabi OS et al [66] reported a prevalence of 27.3% in his comparative study of dry eye in rheumatoid arthritis patients with age matched controls. One reason for this could be that, they considered the Schirmer test result to be positive if it was less than or equal to 5 mm of wetting. When we performed a similar sub grouping in our study, we obtained a prevalence of 28.6% (table 13), which is comparable to the results obtained by them.

Association of dry eye with age:

The total patient sample was divided into 5 sub groups based on their age (Table 2). The prevalence of dry eye was found to significantly increase with the increase in age of the patients (p= 0.028) and was found to be significantly higher in persons aged more than 40 years. This corresponds to the results obtained by Punjabi et al [66] who showed a strong correlation between advancing age and dry eye. In their study, 80% of the patients testing positive for dry eye were aged 40 years or older. In our study, the percentage of patients testing positive for dry eye among the 40-65 year age group was 79.41% .

Sex wise distribution of dry eye:

We found a higher prevalence of dry eye in women compared to men, which corresponded to the findings of other studies (Table 3).

Table 20: Comparative prevalence rates between males and females

Studies	% prevalence of dry eye	
	Females	Males
Our study	85%	15%
Mumbai study [66]	74%	26%

It may be argued that the prevalence of rheumatoid arthritis itself is higher in females compared to males, leading to an increased percentage of those with dry eye too. However, our findings are supported by studies done to assess risk factors and prevalence of dry eye in general population who have found a significantly higher prevalence of dry eye among women compared to men.

Moss et al [67] found a prevalence of 16.7% in women compared to 11.4% in men. These were the prevalence rates obtained after adjusting for age. Sahai et al [68] found a prevalence of 22.8% in women compared to 14.9% in men in his study on hospital based population. Among the 20 patients aged 50 years or older and who tested positive for dry eye, 17 were females. Among the total number of women identified with dry eye, majority i.e 58.6% were in the post menopausal age group.

OSDI scores:

It has been proposed time and again that there is a poor correlation between subjective symptoms and objective signs of dry eye, thus emphasizing the need for objective testing in all patients at risk for developing dry eye. The OSDI scoring system was used in our study as it can classify the dry eye into mild, moderate and severe varieties (Table 5).

An OSDI scoring of 67-100 which corresponds to severe dry eye, was found to correlate significantly with objective tests of dry eye. (p=0.006) . We propose that, in places where the out patient attendance is high, and performing an objective test is not feasible in such a large group, the patients may be screened using the OSDI scoring system and those with higher scores, subjected to objective testing of dry eye. There is a higher probability of detecting dry eye in such patients.

Similar findings were noted by Ozcura et al [69] who evaluated the OSDI questionnaire for diagnosis of dry eye and found a significant inverse correlation between OSDI and TBUT scores. Simpson TL et al [70] have found that this scoring system is highly sensitive in differentiating symptomatic and asymptomatic subjects of dry eye. Srinivasan et al [71] used the OSDI scoring system to detect dry eye in post menopausal women and concluded that OSDI could be effectively used to separate post menopausal women who demonstrate clinical signs of ocular dryness.

We also were able to demonstrate that a large number of patients with dry eye do show symptoms and the symptoms correlate well with signs in cases of severe dry eye though not much in cases of moderate dry eye. Another reason for the low symptoms may be that, most of the patients in our study group were from low socio

economic status with lower literacy rates. These patients were more worried about their systemic symptoms and tend to undermine their ocular symptoms.

RA duration and dry eye:

We divided the patients into subgroups based on duration of rheumatoid arthritis. The prevalence of dry eye was found to increase as the duration of rheumatoid arthritis increased, with the greatest percentage (66.67%) being in those having rheumatoid arthritis for 15 years or longer (Table 6).

Studies done previously have found a greater prevalence of dry eye with longer duration of rheumatoid arthritis. Polanska et al found a statistical connection between the presence of dry eye and duration of rheumatoid arthritis longer than ten years. [24]

However, we were not able to demonstrate a significant statistical correlation between the duration of rheumatoid arthritis and presence or severity of dry eye ($p= 0.784$). The reason for this could possibly be the small sample size of our study. Another reason for this could be that our study considered the duration of rheumatoid arthritis based on history given by the patient whereas other studies have considered duration based on maintained RA registers. Thus it is possible that we could have got wrong values of duration.

Our study did not take into consideration the activity of the disease, and hence we were unable to correlate RA severity with dry eye. However, a significant number of studies assessing ocular symptoms and signs in rheumatoid arthritis have tried to compare dry eye occurrence with activity of rheumatoid arthritis and none of them

have found any correlation between the two. They have proposed that dry eye should be tested for in all patients of rheumatoid arthritis as it is independent of RA activity.

RA factor and dry eye:

There is a higher incidence of extra articular manifestations in those with RA factor positivity, which also is said to indicate a poorer prognosis. In our study, we did not find any statistically significant correlation between the presence of RA factor and occurrence of dry eye though the prevalence of dry eye was found to slightly higher (50%) in the RF positive group compared to the RF negative group (47.8%) (Table 7). Our findings correspond to those of Polanska et al have obtained similar results in their study.[24] Uhlig et al [65] also found that there was no significant difference in presence of rheumatoid factor between sicca and non sicca groups in rheumatoid arthritis.

Matsuo et al ,[22] in their study of ocular complications of rheumatoid arthritis, found that patients with keratoconjunctivitis sicca had a significantly higher titres of rheumatoid factor. We performed a similar analysis (table 8) but were not able to demonstrate any significant difference in the dry eye prevalence between patients with lower and higher titres of rheumatoid factor. The rheumatoid factor positivity among the tested population was also low in our study compared to other studies.

Presence of dry mouth:

We found 17.14% of the study population to have evidence of both dry eye and symptoms of dry mouth (Table 9). Schein et al [57] did a population based assessment of dry eye and dry mouth and found that the dry mouth symptoms increased with age, female sex and white race. Among the patients who reported

symptoms of dry mouth in our study, only one patient was male and rest were females. 70.5% of these patients were aged more than 40 years.

Uhlig T et al [65] observed that among the patients with RA, 50% showed presence of oral sicca symptoms. In our study, 24.2% of the study population reported to have oral sicca symptoms. The lower prevalence in our study could be because of two reasons. Firstly, we had excluded the patients of diabetes which is an independent cause of dry mouth, which was not done in their study. Secondly, the mean age of the patients in their study was higher as was the upper limit of age (70 years), which could have lead to discrepancy as dry mouth symptoms are found to increase with age.

Ocular signs on examination:

Conjunctival congestion and corneal dryness were the most common signs observed (Table 10). 65.6% of the patients with conjunctival congestion showed evidence of dry eye. The association between dry eye and conjunctival congestion was found to be statistically highly significant (p=0.001). Our findings correspond to those of Srinivasan et al [71] who also found an increased incidence of bulbar hyperemia in women with dry eye. It may be used as one of the diagnostic signs for screening for evidence of dry eye instead of directly performing the tests. Corneal dryness, though noted to be high in our study, is subject to inter observer variability and not recommended. We could not find other studies looking for signs of dry eye performed recently.

Refractive errors and dry eye:

We found a significant correlation between the presence of refractive errors and dry eye (p=0.027) (Table 11). Our findings are consistent with other studies (Sahai et al)[68] which have shown that compared to emmetropes, prevalence of dry eye was higher in those with corrected and uncorrected refractive errors. Study by Jie et al [72] has shown that there was a significantly higher incidence of dry eye among people with undercorrected refractive errors. It has been postulated that persons with refractive errors have an increased tendency to rub their eyes which, apart from the introduction of infective material, sebum and sweat, could cause the lodgement of particulate foreign substances into the eye that predispose to tear film instability.[68] Also, people with uncorrected refractive errors have more tendency to sqeeze the eyes, causing instability of tear film, predisposing to dry eye.

Tests performed for detection of dry eye:

Four diagnostic tests were performed on all patients. Positivity in two out of four tests was necessary in order to label the patient as having dry eye. As mentioned earlier, this criteria was adopted for diagnosis in order to increase the detection rate and hence to arrive at an accurate prevalence (Tables 12 - 18).

Among all the tests, Schirmer test was found to be the best one to be done in RA cases as it showed a high sensitivity, specificity and predictive values (positive and negative). Apart from being one of the most frequent tests used in dry eye clinical practice, other studies have also shown it to have a sensitivity and specificity of up to 85% which correspond to the results of our study. [46]

Rose Bengal test was the next best test in terms of sensitivity and specificity (table 17). The characteristic staining of the interpalpebral area in wing shaped manner, was noted in most of the cases who tested positive.

On comparing the results of Schirmer test and Rose Bengal test, it was found that, 27 patients (38.5%) showed positive result for both the tests. 3 patients (4.2%) were positive with Rose Bengal test but negative with Schirmer test. 5 patients (7.1%) were positive with Schirmer test but negative with Rose Bengal test.

TBUT was found to give poor results in our study. The findings of our study correlate with those of Punjabi et al [66] who found the prevalence of dry eye based on this test alone to be 22.62% (our study- 19.11%). One possibility for this may be that, this test is considered to be specific for mucin deficient dry eye whereas the primary type of dry eye occurring in rheumatoid arthritis is the aqueous deficient type.

On performing conjunctival impression cytology, we found 36.7% of the eyes to show grade 2 or grade 3 changes that define dry eye. The sensitivity and specificity of this test was found to be moderate compared to the other tests used in our study. However, it is the best means to detect the morphological changes occurring on the ocular surface in dry eye states. The results of this test were found to correlate well with those of Schirmer test. A significantly larger number of patients with Schirmer values of ≤5mm were found to have grade 2 or grade 3 changes on impression cytology (table 18).

Though the study of conjunctival surface by means of impression cytology has been performed earlier in dry eye syndrome, we could not find any study where this test had been performed in cases of rheumatoid arthritis. Hence we were not able to

compare the results of this test with other studies, to know if the changes occurring are similar. However, in terms of sensitivity of this test as a screening test for dry eye, our results were comparable to those of other studies.

CONCLUSION

- Dry eye is prevalent among rheumatoid arthritis patients and it is more common in those with longer duration of rheumatoid arthritis.

- The symptoms of dry eye of severe degree correlate well with the signs only when severe and dry eye has been found to cause damage to the ocular surface epithelium even in the absence of symptoms.

- Recent advances in understanding the pathophysiology of dry eye have revolutionized the treatment options which can increase patient comfort.

All these factors reinforce the need for early detection of dry eye in rheumatoid arthritis patients by means of screening tests, as simple as a Schirmer test. While considering a diagnosis of dry eye, attention should also be paid to other factors such as age of the patient, gender and presence of refractive error, as dry eye has a positive correlation with these factors.

Early detection and treatment of dry eye will go a long way in improving the quality of life of these patients.

SUMMARY

- Among 70 patients of rheumatoid arthritis studied, prevalence rate of dry eye was found to be as high as 48.5%. It formed a major chunk of ocular manifestations of rheumatoid arthritis.

- The occurrence of dry eye increased with the increased duration of rheumatoid arthritis.

- There was no relationship between the presence of rheumatoid factor or RF titres and dry eye occurrence and severity.

- The prevalence of dry eye increased with increase in age and was significantly higher among people more than 40 years of age.

- Prevalence was higher among females when compared to males, especially among those in post menopausal age group.

- Conjunctival congestion was found to be a reliable sign of dry eye with a strong positive association.

- People with refractive errors, with or without history of spectacle use, had a higher incidence of dry eye compared emmetropes.

- OSDI was found to be a reliable measure of dry eye symptoms. Higher scores of OSDI, indicating severe dry eye, correlated well with the diagnostic tests for dry eye.

- Schirmer test was the best test for detecting dry eye in rheumatoid arthritis patients with a high sensitivity and specificity, followed by rose bengal test and impression cytology. TBUT had low sensitivity.

- Impression cytology was a reliable measure for detecting ocular surface changes occurring in these dry eye patients. Majority of these patients showed grade 2 or grade 3 changes. These changes were more among those with Schirmer score lower than 5 mm.

- In rheumatoid arthritis,17.14% of the patients had history of dry mouth also along with dry eyes. These patients need to be evaluated further for definitive diagnosis of Sjogren's syndrome.

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PROFORMA

NAME OF THE PARTICIPANT:

AGE :

SEX:

ADDRESS:

DURATION OF RHEUMATOID ARTHRITIS:

H/O DIABETES: yes no

H/O CONTACT LENS USE: yes no

H/O THYROID DISEASE: yes no

H/O SPECTACLE USE yes no

IF YES, DURATION:

H/O DRY MOUTH yes no

RA FACTOR: positive negative

Titres

ANA positive negative not applicable

IB (for SSA/SSB) positive negative not applicable

SYMPTOMS OF DRY EYE:

(Ocular Surface Disease Index- OSDI questionnaire)

Have you experienced any of the

following in the past one week ?

	All the time	Most of the time	Half the time	Some times	Never
1) Eyes that are sensitive to light					
2) Eyes that feel gritty					
3) Painful or sore eyes					
4) Blurred vision					
5) Poor vision					
Have the problems with your eyes limited you in performing any of the following in the past one week ?	All the time	Most of the time	Half the time	Some times	Never
6) Reading					
7) Driving at night					
8) Working with computer or bank machine					
9) Watching TV					
Have your eyes felt uncomfortable in any of the following situations during the last week ?	All the time	Most of the time	Half the time	Some times	Never
10) Windy conditions					
11) Places or areas with low humidity					
12) Areas that are air conditioned					

*Values to determine dry eye disease severity calculated using the OSDI© formula:
OSDI©= (sum of scores) x 25 / (No. of questions answered)

OCULAR EXAMINATION:

	RIGHT EYE	LEFT EYE
VISUAL ACUITY		
PIN HOLE		
WITH GLASSES		
VISUAL AXIS		
EXTRA OCULAR MOVEMENTS		
ADNEXA		
Eye lids		
Eye lashes		
Meibomian gland openings		
Lacrimal puncta		
CONJUNCTIVA		
Palpebral		
Bulbar		
Congestion		
Chemosis		

CORNEA

SCLERA

ANTERIOR CHAMBER

IRIS

PUPIL

LENS

FUNDUS

INVESTIGATIONS:

	Right eye	Left eye
1) SCHIRMER TEST		
2)TEAR FILM BREAK UP TIME		
3)ROSE BENGAL TEST		
4) IMPRESSION CYTOLOGY		

DIAGNOSIS:

INFORMED CONSENT FORM FOR STUDY OF DRY EYE IN

RHEUMATOID ARTHRITIS PATIENTS

Mr./Ms./Mrs.----------, we are requesting you to enroll yourself in the study titled " Study of Dry eye in Rheumatoid arthritis patients"conducted by Dr. CHAITRA K.L, post graduate student in M.S.Ophthalmology under the guidance of Dr. R.K.DANDUR at J.N.Medical college, Belgaum under KLE University, Belgaum.

Tear film is an important part of eye. Loss of tear film due to any cause gives rise to a condition known as dry eye. This study is being undertaken to know, to what extent this dry eye may occur in patients of rheumatoid arthritis. 70 patients of rheumatoid arthritis coming to KLES Dr. Prabhakar Kore hospital will be participating in this study. You are requested to participate in research because you are into the study group.

PROCEDURE INVOLVED:

The participants are required to answer a few questions regarding symptoms of dry eye . 4 tests will be conducted on them to assess the damage which may have occurred to the outer covering of the eyeball. 4 types of strips will be put into the eye at different times for the study. These tests will be done by experienced doctors.

RISKS & BENEFITS:

The instillation of one of the strips and eye drops into the eye may cause some amount of burning sensation which will come down on its own and will not require any special treatment. It will not cause any harm to the eye.

By doing these tests, dry eye which might occur in you can be detected in early stages. By this, further damage to cornea,conjunctiva and complications which are likely to occur can be prevented.

You will not be required to spend any money for this eye examination. The tests will be done free of cost. You will also not receive any free gifts or money for participating in the study.

ALTERNATIVES:

You will be participating in this study by your own free will. Your decision to participate or not in the study will not affect the treatment given to you in the hospital.

PRIVACY & CONFIDENTIALITY:

The only people to know that you are a research subject are members of the research team. No information about you or provided by you during the research will be disclosed to others without your written permission except:

1. In emergency to protect your rights and welfare.

2. If required by law

AUTHORISATION TO PUBLISH RESULTS:

The results of this study may be published for medical purposes or given to scientific groups for further research. Your identity will not be revealed at any time.

In case you have any questions related to the study , you can contact Dr. Chaitra K.L. (Phone No.9480157981).

In case you have any questions about your rights as a study participant , you can contact Dr. V.D.Patil (0831-2471350)

CONSENT STATEMENT:

I undersigned---------- am participating in this study by my own free will. I have the right to withdraw from the study at any time due to any reason. I have read the consent form /had it read out to me in front of witnesses and have understood it. I have the right to ask questions at any time during the study.

Signature of the participant. Date

Name:

Thumb impression

Signature of the witness Date

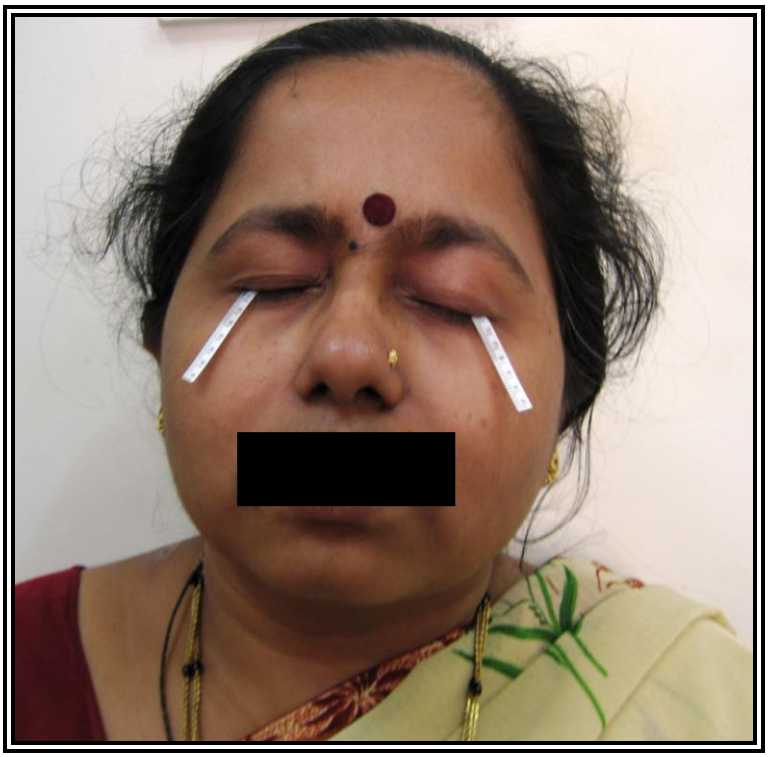
Name :

Name of the investigator Date

Signature: Place

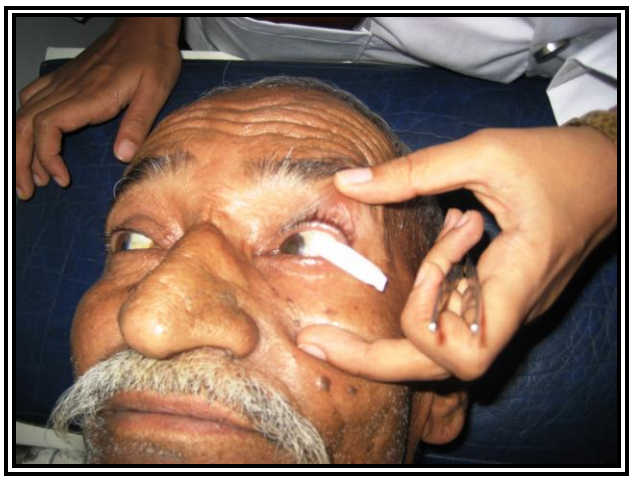
PHOTOGRAPHS

Colour Plate 1: Schirmer, Rose Bengal, Fluorescein strips, Cellulose acetate strip, Glass rod, Forceps used for dry eye assessment



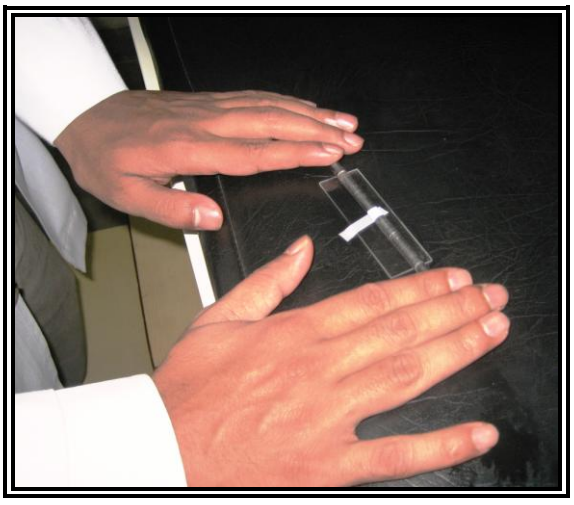
Colour Plate 2: Schirmer test bring performed on middle aged female patient

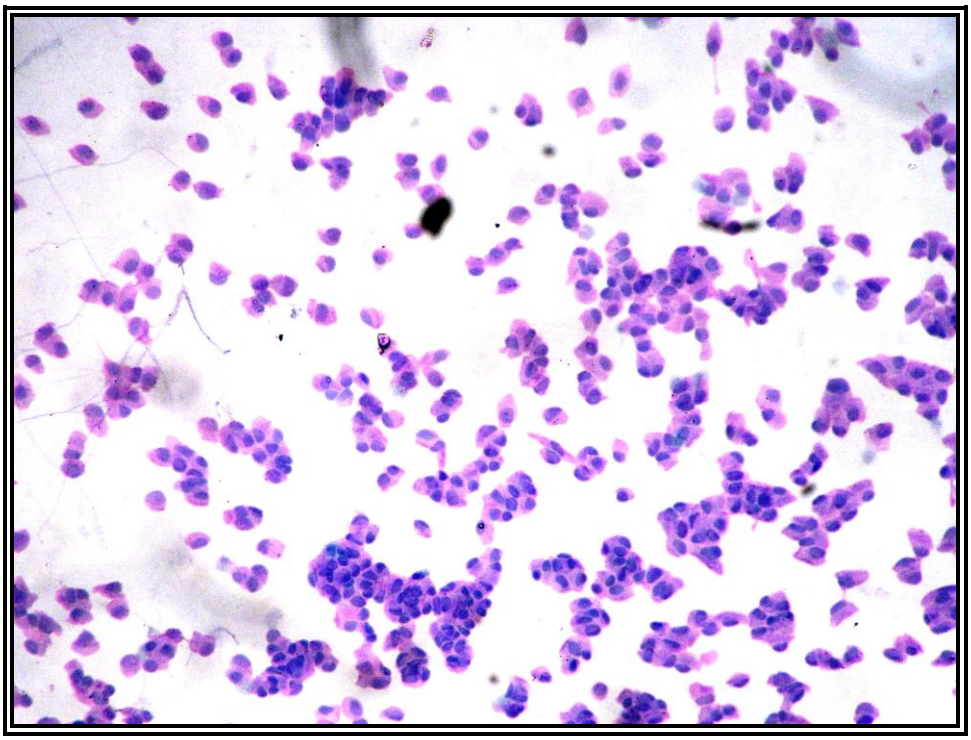
Colour Plate 3: Rose Bengal staining in a patient with severe dry eye



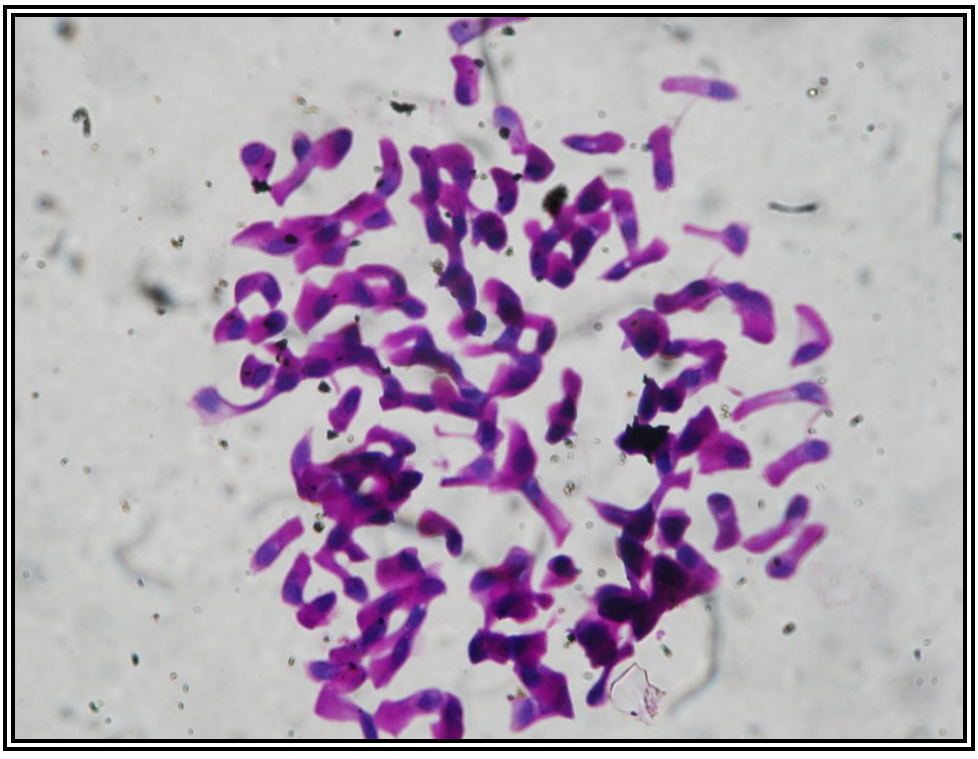
Colour Plate 4: Conjunctival impression being taken using Cellulose acetate strips

Colour Plate 5: Transfer of impression to glass slide

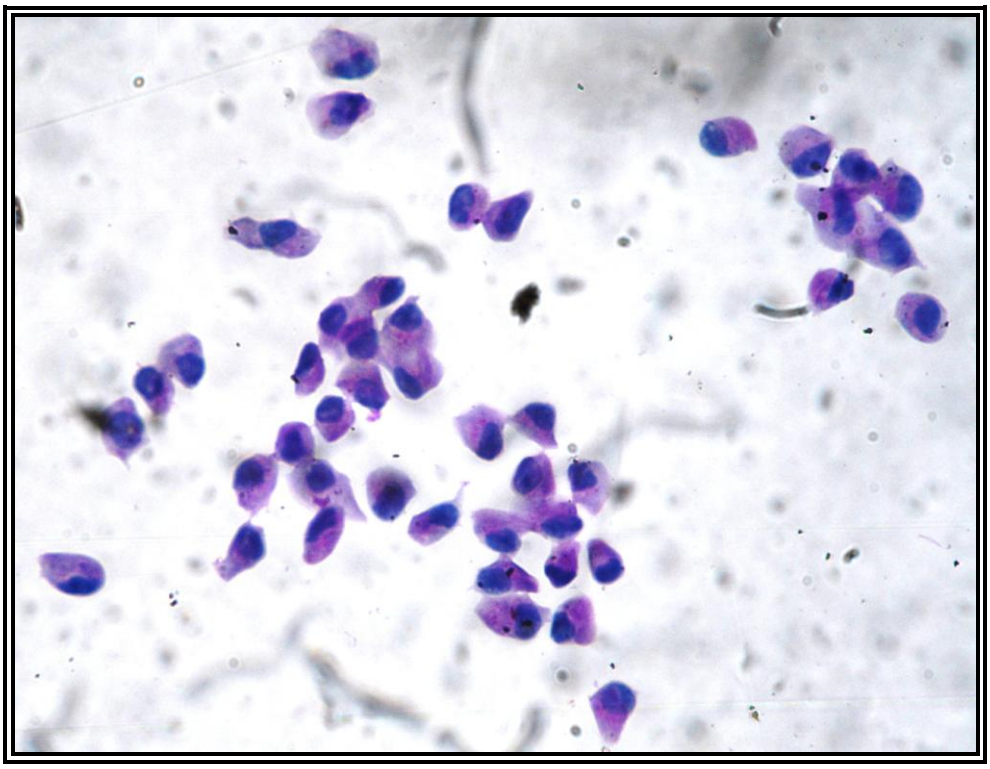




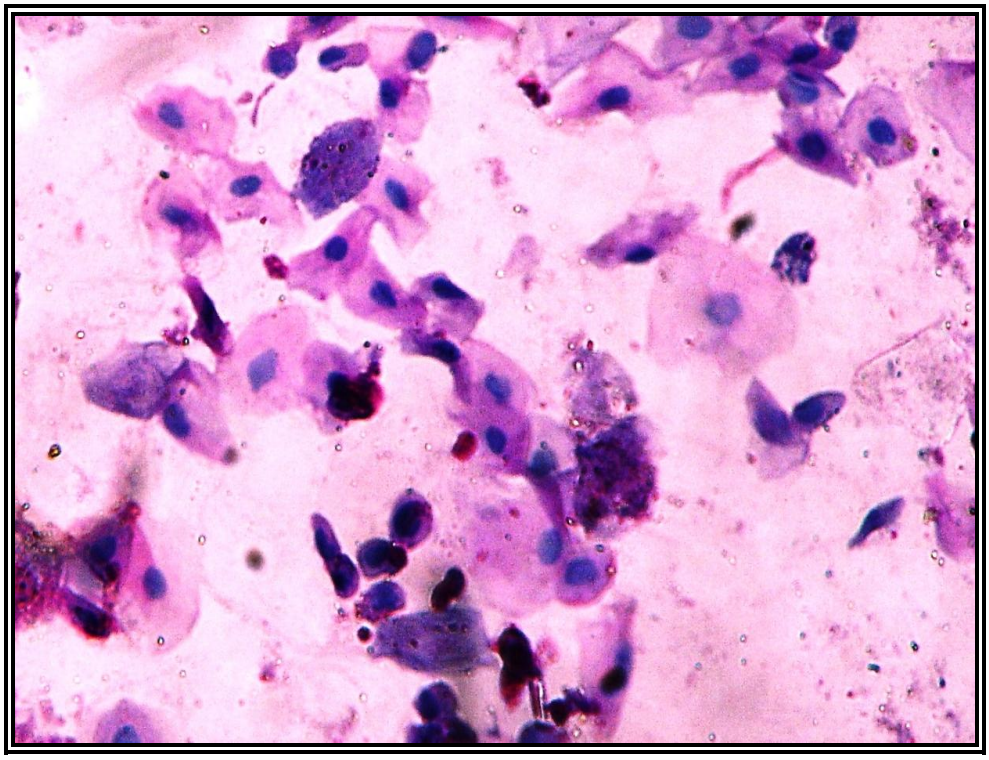
Colour Plate 6: Photomicrograph showing normal conjunctival cells (low power view)



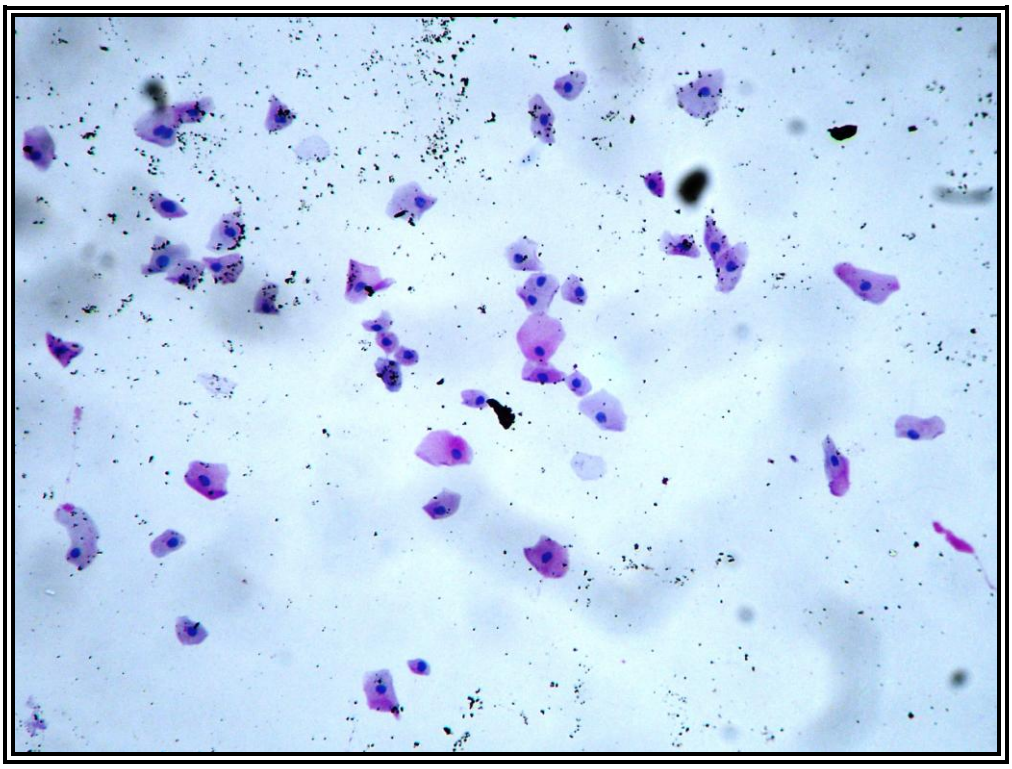
Colour Plate 7: Photomicrograph showing normal conjunctival epithelial cells and goblet cells (high power view)



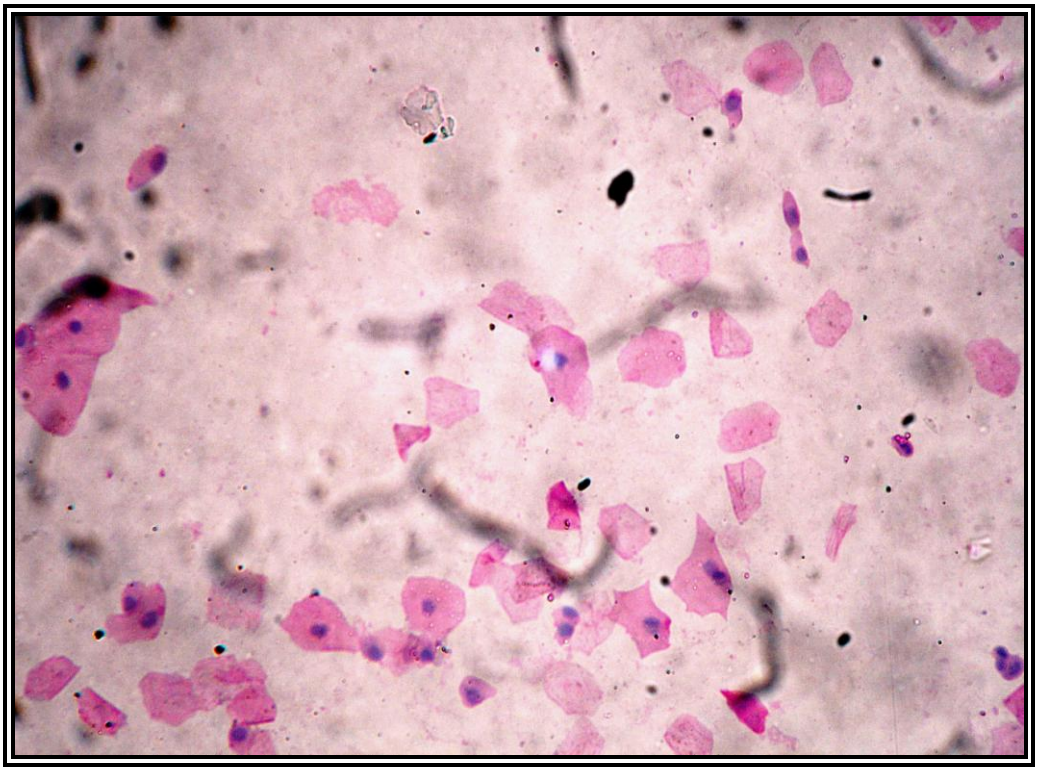
Colour Plate 8: Photomicrograph showing conjunctival impression cytology Grade -0



Colour Plate 9: Photomicrograph showing conjunctival impression cytology Grade -1



Colour Plate 10: Photomicrograph showing conjunctival impression cytology Grade -2



Colour Plate 11: Photomicrograph showing conjunctival impression cytology Grade -3

MASTER CHART

PATIENT NO.	INITIALS	AGE	SEX	RAD(YRS)	SPECKS/DURATION	DRY MOUTH	RF/TITRES	OSDI SCORES	BCVA	ADNEXA	CONJUNCTIVA	CORNEA	SCLERA	AC/IRIS/PUPIL	LENS	FUNDUS	SCHIRMER (mm)	TBUT (sec)	ROSE BENGAL	CIC GRADE	DRY EYE
1	JA L	65	F	5	Y /5 YRS	N	Ng	43.75	6 BY 18	NM	D	CLEAR	NM	NM	CTC	NM	3	10	7	2	PRESENT
	JA R								6 BY 18	NM	D	CLEAR	NM	NM	CTC	NM	3	10	7	2	PRESENT
2	MB R	50	F	2	N	Y	Ng	30.55	6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	2	12	4	2	PRESENT
	MB L								6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	2	12	8	2	PRESENT
3	AK R	31	M	1	N	N	Ng	57.5	6 BY 9	NM	C	V	NM	NM	NM	NM	20	10	2	2	ABSENT
	AK L								6 BY 12	NM	C	V	NM	NM	NM	NM	20	10	6	2	ABSENT
4	AB R	63	F	10	N	N	Ng	8.33	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	10	12	0	0	ABSENT
	AB L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	20	14	0	0	ABSENT
5	IG R	61	F	2	Y/2YRS	Y	P/ 320	27.77	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	3	10	0	2	PRESENT
	IG L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	5	10	0	2	PRESENT
6	CK R	55	F	3 M	N	Y	Ng	5.55	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	4	10	0	2	PRESENT
	CK L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	21	10	0	0	ABSENT
7	LS R	35	F	4 M	Y/2YRS	N	Ng	17.5	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
	LS L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT

8	AN R	38	F	3	N	Y	Ng	8.33	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	20	0	1	ABSENT
	AN L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	20	0	0	ABSENT
9	MH R	40	F	10	N	Y	Ng	16.66	6 BY 6	NM	SCH	CLEAR	NM	NM	NM	NM	16	12	0	0	ABSENT
	MH L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	17	12	0	0	ABSENT
10	GK L	61	M	13	Y/5YRS	N	P/ 160	25	6 BY 6	NM	C	CLEAR	THIN	NM	NM	NM	12	13	4	2	PRESENT
11	SV R	36	M	1	N	N	P /320	0	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	1	ABSENT
	SV L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	1	ABSENT
12	BM R	65	F	1	Y/ 18YRS	Y	P /160	69.4	6 BY 12	NM	C	O	NM	NM	CTC	NM	16	8	4	2	PRESENT
	BM L								6 BY 12	NM	C	CLEAR	NM	NM	CTC	NM	5	7	4	2	PRESENT
13	SM R	40	F	1.5	N	N	Ng	0	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
	SM L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
14	LX R	62	F	4	Y/ 1.5YRS	N	P /250	72.22	6 BY 6	NM	C	CLEAR	C	NM	NM	NM	2	8	10	2	PRESENT
	LX L								6 BY 9	NM	C	CLEAR	C	NM	NM	NM	2	8	8	2	PRESENT
15	KN R	45	F	6 M	Y/ 0.5YRS	N	P /180	11.11	6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
	KN L								6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
16	NB R	40	F	1	N	N	P /160	22.22	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	2	10	0	0	ABSENT
	NB L								6 BY 6	NM	PT	CLEAR	NM	NM	NM	NM	25	10	0	0	ABSENT
17	NJ R	25	M	1	N	N	Ng	25	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
	NJ L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
18	SK R	25	F	4 M	N	N	Ng	0	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
	SK L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
19	VK R	52	F	2	Y/ 5YRS	Y	Ng	19.44	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	8	0	2	PRESENT
	VK L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	10	0	2	ABSENT
20	NIN R	40	F	3 M	N	Y	Ng	43.75	6 BY 6	NM	NM	D	NM	NM	NM	NM	1	10	9	2	PRESENT
	NIN L								6 BY 6	NM	NM	D	NM	NM	NM	NM	2	12	8	2	PRESENT

21	JB R	60	M	9 M	Y/7YRS	N	Ng	19.44	6 BY 6	NM	NM	D	NM	NM	NM	NM	4	10	6	1	PRESENT
	JB L								6 BY 6	NM	NM	D	NM	NM	NM	NM	5	10	6	1	PRESENT
22	LG R	45	F	9	Y/3YRS	Y	Ng	30.55	6 BY 6	NM	NM	CLEAR	THIN	NM	CTC	NM	6	12	0	2	PRESENT
	LG L								CF IM	NM	NM	CLEAR	THIN	NM	CTC	EX	20	15	0	1	ABSENT
23	AD R	40	M	1 M	N	N	Ng	13.64	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	20	12	3	0	ABSENT
	AD L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	20	12	3	0	ABSENT
24	DS R	39	F	2	Y/4YRS	N	Ng	25	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	3	0	ABSENT
	DS L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	12	0	0	ABSENT
25	TS R	22	F	5	Y/1YR	Y	Ng	44.44	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
	TS L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
26	MM R	50	F	10	N	N	Ng	19.44	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	17	12	0	0	ABSENT
	MM L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	17	13	0	0	ABSENT
27	SB R	60	F	4	Y/ 20YRS	N	Ng	21.88	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	0	ABSENT
	SB L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	12	0	0	ABSENT
28	RK R	42	F	6	Y/1YR	N	P /4+	30.56	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	6	12	4	2	PRESENT
	RK L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	6	12	0	2	PRESENT
29	PH R	61	F	2	Y/5YRS	N	Ng	5.56	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	5	10	10	2	PRESENT
	PH L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	5	10	10	2	PRESENT
30	MS R	40	M	2	Y/3YRS	N	Ng	0	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	20	13	0	0	ABSENT
	MS L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	20	12	0	0	ABSENT
31	IS R	40	F	6	N	N	Ng	3.13	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	13	0	0	ABSENT
	IS L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	13	0	0	ABSENT
32	KK R	50	F	1	N	N	P /20	6.25	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	9	13	4	1	PRESENT
	KK L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	9	13	3	1	ABSENT
33	ST R	60	M	15	Y/ 10YRS	Y	Ng	19.44	6 BY 12	NM	C	V	NM	NM	CTC	NM	2	8	6	2	PRESENT
	ST L								6 BY 9	NM	C	V	NM	NM	NM	NM	2	7	8	2	PRESENT

34	SS R	48	F	4	Y/3YRS	N	Ng	16.67	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	0	ABSENT
	SS L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	15	0	0	ABSENT
35	AP R	46	F	3	Y/1YR	Y	Ng	77.78	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	20	10	0	0	ABSENT
	AP L								6 BY 9	NM	C	CLEAR	NM	NM	NM	NM	9	8	6	3	PRESENT
36	LA R	60	F	9	Y/5YRS	N	Ng	2.78	6 BY 9	NM	D	CLEAR	NM	NM	NM	NM	6	14	6	3	PRESENT
	LA L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	9	19	0	0	ABSENT
37	AN R	52	F	15	N	N	P /320	12.5	6 BY 6	NM	D	CLEAR	NM	NM	NM	NM	4	12	8	1	PRESENT
	AN L								6 BY 6	NM	D	CLEAR	NM	NM	NM	NM	5	12	7	1	PRESENT
38	KMK R	60	F	4	Y/2YRS	N	Ng	8.33	6 BY 6	NM	PT	PT	NM	NM/ NV	NM	NM	4	12	6	2	PRESENT
	KMK L								6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	13	15	3	1	ABSENT
39	UB R	65	F	19	Y/ 10YRS	N	Ng	19.44	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	13	12	0	0	ABSENT
	UB L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	12	0	0	ABSENT
40	NN R	53	F	6	Y/3YRS	N	Ng	25	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	6	8	4	2	PRESENT
	NN L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	10	10	4	2	PRESENT
41	YP R	40	M	2	Y/1YR	N	Ng	22.22	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	8	8	6	2	PRESENT
	YP L								6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	6	6	6	2	PRESENT
42	KC R	40	F	4	Y/ 10YRS	N	P /80	44.44	6 by 9	NM	C	CLEAR	NM	NM	NM	NM	20	15	0	0	ABSENT
	KC L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	25	12	0	0	ABSENT
43	SD R	44	F	9	N	N	P /40	5.55	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	30	0	0	ABSENT
	SD L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	16	0	0	ABSENT
44	SN R	50	F	4	Y/5YRS	N	P /160	34.37	6 BY 9	EXOT ROPIA	C	CLEAR	BLEB	S/PI, AT/	CTC	NM	16	12	0	2	ABSENT
	SN L								6 BY 12	NM	C	CLEAR	BLEB	NM/ PS	CTC	NM	25	15	0	2	ABSENT

45	SH R	52	F	5	N	Y	P /160	52.77	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	4	12	4	2	PRESENT
	SH L								6 BY 9	NM	C	CLEAR	NM	NM	NM	NM	6	13	6	2	PRESENT
46	LM R	44	F	6M	Y/1YR	N	P /80	16.66	6 BY 6	NM	C	D	NM	NM	NM	NM	3	5	7	2	PRESENT
	LM L								6 BY 6	NM	C	D	NM	NM	NM	NM	5	9	5	2	PRESENT
47	LH R	61	F	5	Y/5YRS	N	P /160	6.25	6 BY 9	NM	C	D	NM	NM	NM	NM	3	6	6	2	PRESENT
	LH L								6 BY 36	NM	C	D	NM	NM/ NV	CTC	NM	1	3	7	2	PRESENT
48	SA R	39	F	4	N	N	P /320	88.88	6 BY 6	SB	C	D	NM	NM	NM	NM	1	5	8	2	PRESENT
	SA L								6 BY 6	SB	C	D	NM	NM	NM	NM	2	6	7	2	PRESENT
49	NHB L	60	F	8	N	N	Ng	50	HMCF	NM	NM	CLEAR	NM	NM	CTC	NM	25	12	0	0	ABSENT
50	MBS L	51	F	8	Y/5YRS	N	Ng	25	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	25	15	0	0	ABSENT
51	ME R	30	F	1.5	N	Y	P /320	37.5	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	2	ABSENT
	ME L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	12	0	0	ABSENT
52	RR R	35	F	4	N	N	Ng	2.77	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	5	6	0	1	PRESENT
	RR L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	8	7	0	1	PRESENT
53	VM R	57	F	2	Y/6YRS	Y	P /160	6.25	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	7	14	6	1	PRESENT
	VM L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	13	15	3	1	ABSENT
54	SSN R	63	F	4	Y/4YRS	N	Ng	9.37	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	0	ABSENT
	SSN L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	0	ABSENT
55	GAN R	54	F	5	Y/5YRS	N	Ng	2.77	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	0	ABSENT
	GAN L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	12	0	0	ABSENT
56	SVK R	48	F	11M	Y/ 10YRS	N	Ng	9.37	6 BY 6	BL	NM	CLEAR	NM	NM	NM	NM	5	12	4	2	PRESENT
	SVK L								6 BY 6	BL	NM	CLEAR	NM	NM	NM	NM	13	12	4	1	ABSENT
57	INB R	55	F	2	Y/1YR	N	Ng	5.55	6 BY 9	NM	C	CLEAR	NM	NM	NM	NM	5	6	8	1	PRESENT
	INB L								6 BY 9	NM	C	CLEAR	NM	NM	NM	NM	5	7	8	2	PRESENT

58	AAM R	53	F	8	Y/7YRS	Y	P /3+	31.25	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	12	0	0	ABSENT
	AAM L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	0	ABSENT
59	TBK R	45	F	5	Y/2YRS	Y	Ng	43.75	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	10	10	4	1	ABSENT
	TBK L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	8	10	4	1	PRESENT
60	RSL R	45	M	10	N	N	P /320	0	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	25	12	0	0	ABSENT
	RSL L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	15	15	0	0	ABSENT
61	MCC R	60	M	1	Y/3YRS	N	Ng	33.33	6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	18	15	0	0	ABSENT
	MCC L								6 BY 9	NM	NM	CLEAR	NM	NM	NM	NM	20	14	0	0	ABSENT
62	SSL R	35	M	1	N	N	Ng	12.5	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	7	8	6	2	PRESENT
	SSL L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	3	6	8	2	PRESENT
63	STA R	43	F	5	N	N	P /320	5.55	6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	20	10	0	0	ABSENT
	STA L								6 BY 6	NM	C	CLEAR	NM	NM	NM	NM	22	10	0	0	ABSENT
64	NGA R	60	F	3	N	N	P /1:32	40.62	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	4	11	0	0	ABSENT
	NGA L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	9	12	0	0	ABSENT
65	MNK R	21	M	2	Y/ 10YRS	N	Ng	47.5	6 BY 18	NM	NM	CLEAR	NM	NM	NM	NM	30	12	0	0	ABSENT
	MNK L								6 BY 18	NM	NM	CLEAR	NM	NM	NM	NM	30	11	0	0	ABSENT
66	MVM R	40	F	2	N	N	Ng	0	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	12	0	0	ABSENT
	MVM L								6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	13	0	0	ABSENT
67	GLK R	54	F	12	Y/ 10YRS	N	Ng	87.5	CF 1/2M	NM	C	D	NM	NM	CTC	NM	4	7	7	3	PRESENT
68	RBH R	65	F	6	Y/3YRS	N	P /320	25	6 BY 9	NM	NM	D	NM	NM	NM	NM	6	10	6	2	PRESENT
	RBH L								6 BY 9	NM	NM	D	NM	NM	NM	NM	7	12	6	0	PRESENT
69	BG R	31	F	8	N	N	Ng	75	6 BY 6	NM	D	D	NM	NM	NM	NM	1	3	9	0	PRESENT
	BG L								6 BY 6	NM	D	D	NM	NM	NM	NM	3	4	9	0	PRESENT
70	SSE R	60	F	1.5	N	N	Ng	8.33	6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	14	0	0	ABSENT
	SSE L						Ng		6 BY 6	NM	NM	CLEAR	NM	NM	NM	NM	30	15	0	0	ABSENT

KEY TO MASTER CHART:

AT	ATROPHY
BL	BLEPHARITIS
BCVA	BEST CORRECTED VISUAL ACUITY
C	CONGESTION
CIC	CONJUNCTIVAL IMPRESSION CYTOLOGY
CTC	CATARACT
D	DRY
EXO	EXOTROPIA
F	FEMALE
M	MALE
N	NO
Ng	NEGATIVE
NM	NORMAL
NV	NAEVUS
O	OPACITY
P	POSITIVE
PT	PTERYGIUM
PS	POSTERIOR SYNECHIAE
PI	PERIPHERAL IRIDECTOMY
RAD	RHEUMATOID ARTHRITIS DURATION
S	SHALLOW
SB	SEBORRHOEA
TBUT	TEAR FILM BREAK UP TIME
V	VASCULARIZATION
Y	YES
YRS	YEARS