

**EVALUATION OF CYCLOSPORINE AND PAROTID  
DUCT TRANSPOSITION FOR MANAGEMENT OF  
KCS IN DOGS**

**By**

**ANMOL WATAL  
(J-17-MV-513)**

**Thesis submitted to  
Faculty of Postgraduate Studies  
in partial fulfillment of the requirements  
for the degree of**

**MASTER OF VETERINARY SCIENCE**

**IN**

**VETERINARY SURGERY AND RADIOLOGY**



**Division of Veterinary Surgery and Radiology  
Sher-e Kashmir University of Agricultural Sciences & Technology of Jammu  
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**2019**

DEDICATED

TO

MY BELOVED  
GRANDFATHER

LATE SHR. ROSHAN LAL KHAR

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This is to certify that the thesis entitled "Evaluation of cyclosporine and parotid duct transposition for management of KCS in dogs" submitted in partial fulfillment of the requirements for the degree of M.V.Sc. in subject of **Veterinary Surgery and Radiology**, is a record of bonafide research, carried out by **Anmol Watal**, Registration No. **J-17-MV-513** under my supervision and guidance. No part of the thesis has been submitted for any other degree or diploma.

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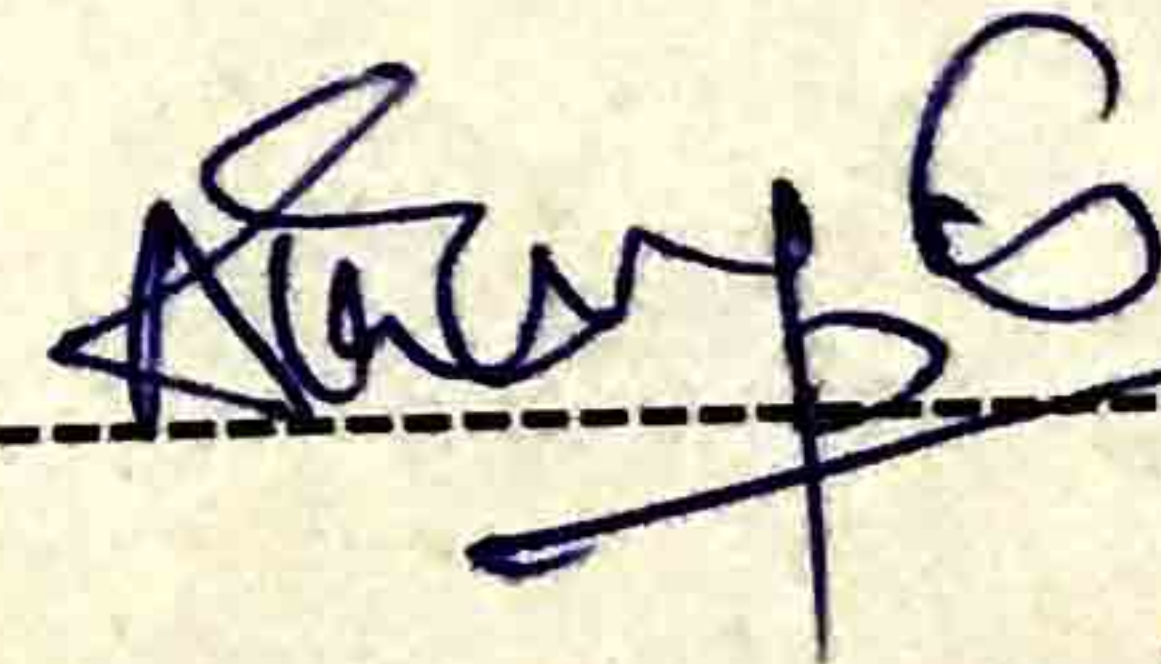
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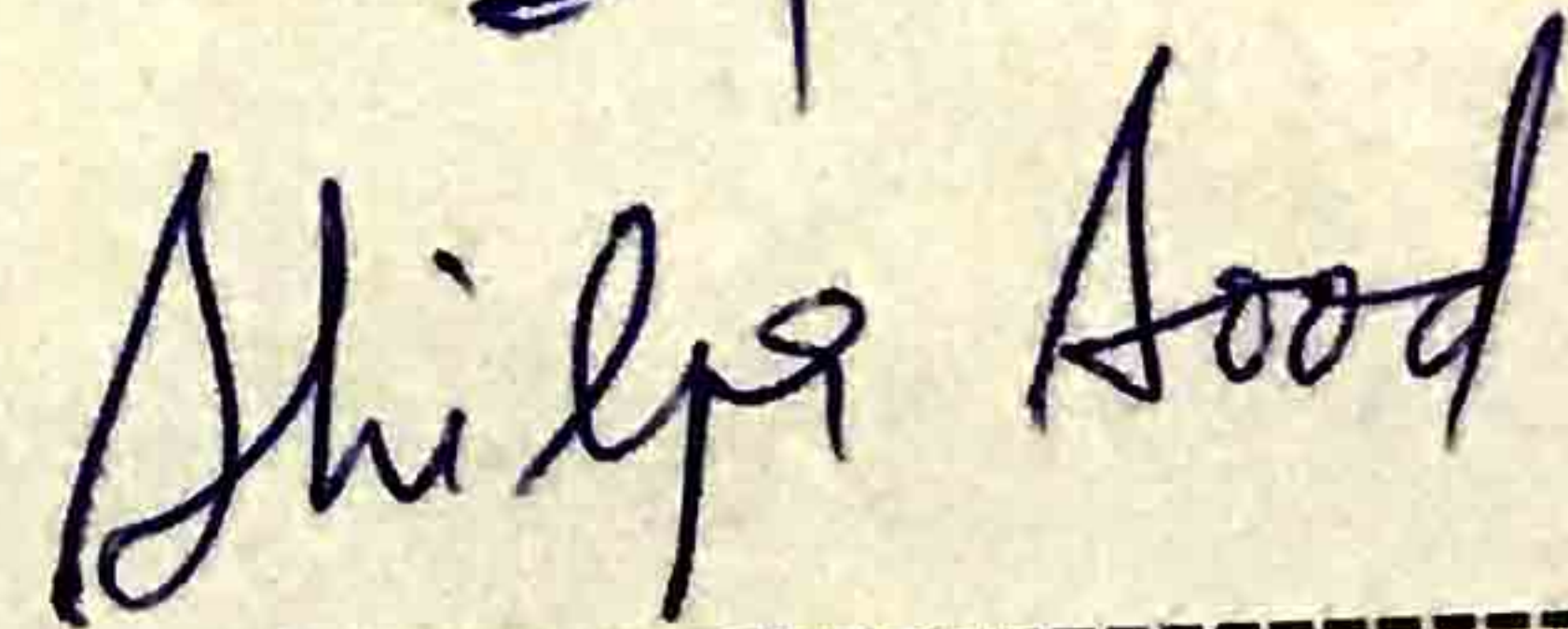
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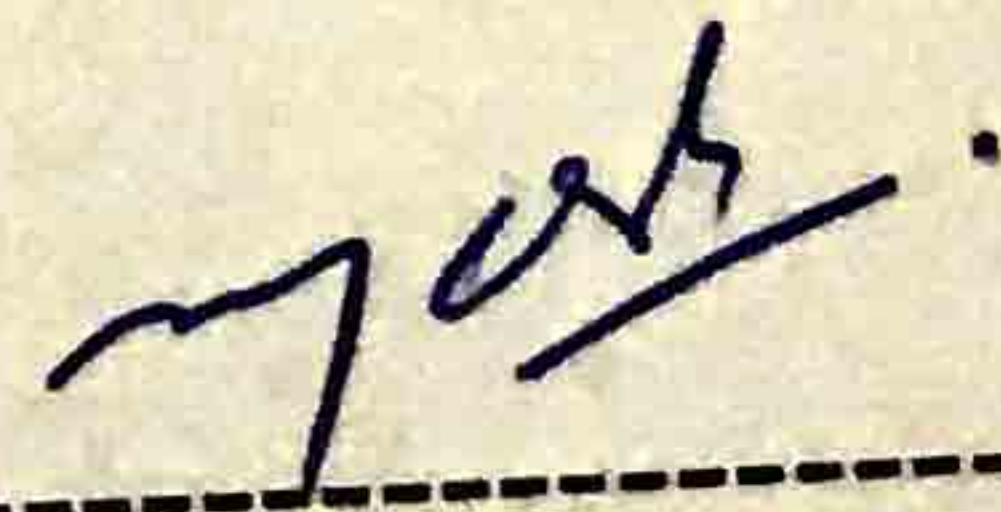


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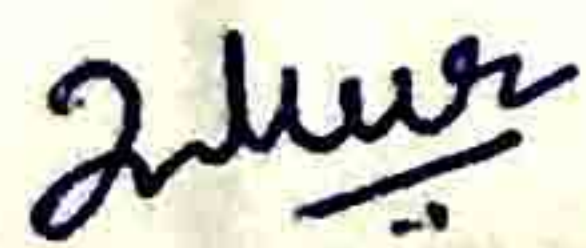
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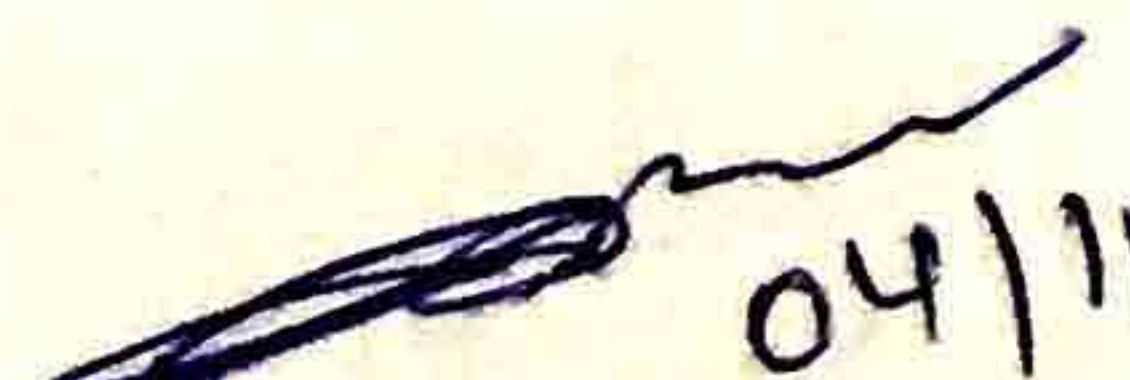
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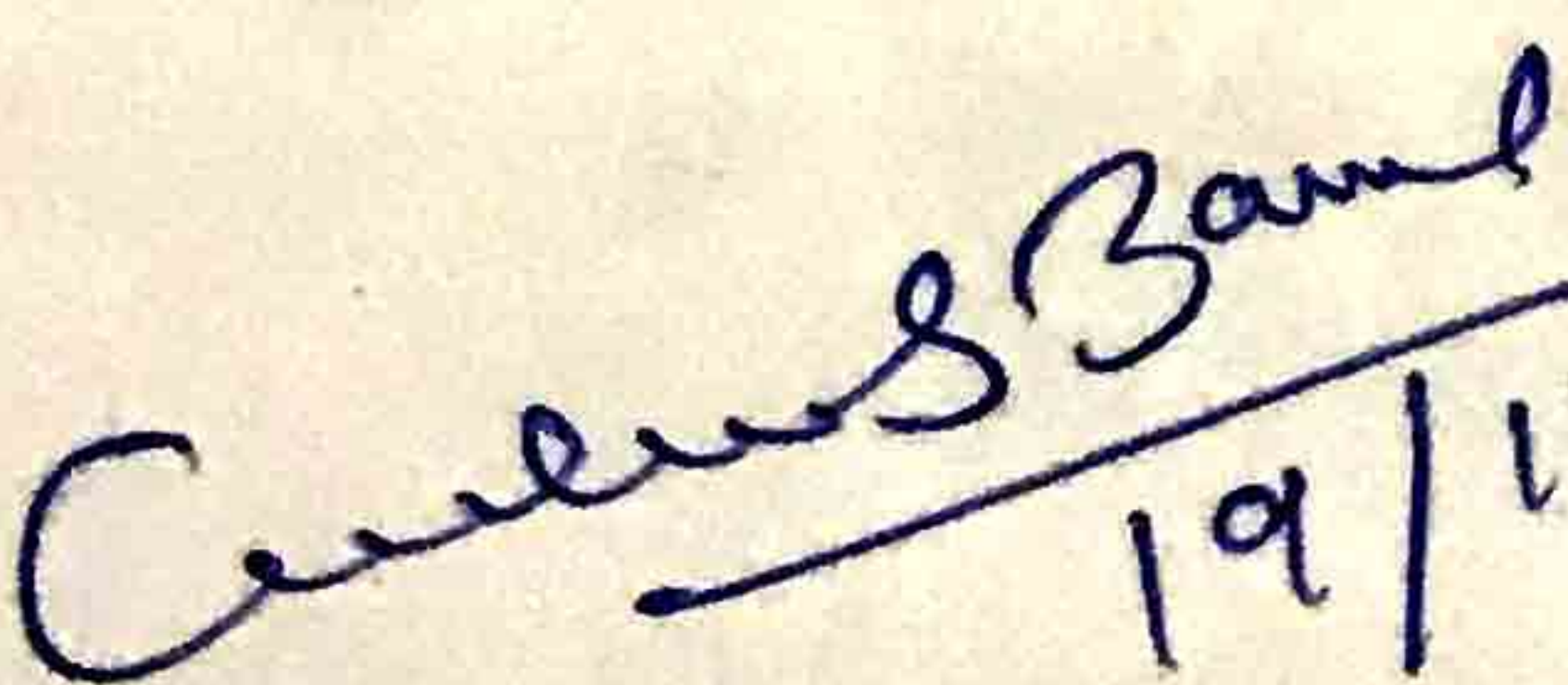
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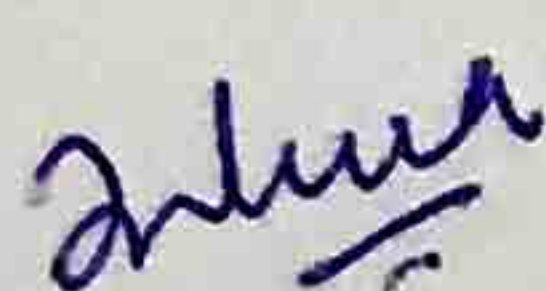
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**ABSTRACT**

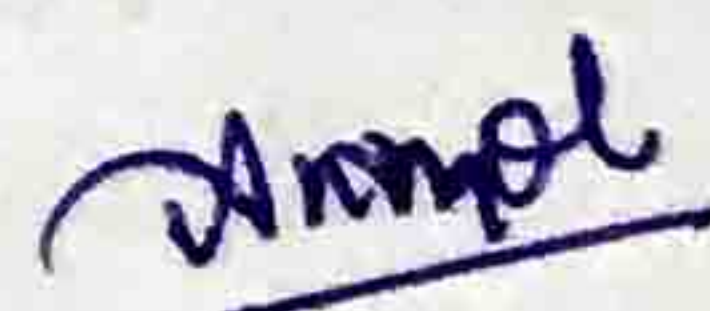
The present study was conducted on ten dogs of either sex affected with Kerato-conjunctivitis sicca (KCS). During the one year study period, 63 canine cases were reported for ocular problems, among which 22 (34.92%) clinical cases were diagnosed as KCS by Schirmer tear test (STT) and only 10 were included in the study. Male dogs (70%) and Pugs (70%) were predominantly affected. Left eye (60%) was affected more and muco-purulent discharge was noted in 50% of the affected cases. All the physiological, hemato-biochemical parameters were within normal reference range in both the groups throughout the study period.

The presented cases were randomly assigned two treatment groups of five dogs each and managed by topical ophthalmic cyclosporine (2mg/gm) and Parotid duct transposition (PDT). Schirmer tear test (STT-I and II) and Tear film breakup time (TFBUT) were estimated in all the cases of canine kerato-conjunctivitis sicca (n=10) which showed a significant decrease in the affected dogs as the treatment progressed. Improvement in neuro-ophthalmic tests, congestion, photophobia, ocular discharge was also seen post-treatment. Antibiotic sensitivity revealed 100% sensitivity to gentamicin and intermediate sensitivity to moxifloxacin. Medication with cyclosporine improved the vision, decreased the conjunctivitis, mucous discharge and significantly improved the precorneal tear film but life long therapy is suggested. PDT was a successful procedure based on the improvement in STT and TFBUT results but was associated with minor complications. It is therefore, recommended that PDT should be used as a treatment option for restoring the ocular surface health for KCS in dogs especially when owner compliance is poor.

**Keywords:** Kerato-conjunctivitis sicca, Cyclosporine, Parotid duct transposition.



**Signature of Major Advisor**



**Signature of the student**

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## ABBREVIATIONS AND SYMBOLS USED

<b>ABST</b>	<b>Antibiotic sensitivity test</b>	<b>n</b>	<b>Number</b>
<b>B</b>	<b>Basophil</b>	<b>PLR</b>	<b>Pupillary light reflex</b>
<b>b.i.d.</b>	<b>Twice in a day</b>	<b>PTF</b>	<b>Precorneal tear film</b>
<b>Cm</b>	<b>Centimeters</b>	<b>PDT</b>	<b>Parotid duct transposition</b>
<b>dl</b>	<b>Decilitre</b>	<b>°F</b>	<b>Degree Fahrenheit</b>
<b>DLC</b>	<b>Differential leukocyte count</b>	<b>q<sup>12 hr</sup></b>	<b>Every 12 hours</b>
<i>et al</i>	<b>and others</b>	<b>q.i.d</b>	<b>Four times a day</b>
<b>E</b>	<b>Eosinophil</b>	<b>RR</b>	<b>Respiration rate</b>
<b>Fig.</b>	<b>Figure</b>	<b>RT</b>	<b>Rectal temperature</b>
<b>Hb</b>	<b>Haemoglobin</b>	<b>SE</b>	<b>Standard error</b>
<b>HR</b>	<b>Heart rate</b>	<b>STT</b>	<b>Schirmer tear test</b>
<b>KCS</b>	<b>Kerato conjunctivitis sicca</b>	<b>TFBUT</b>	<b>Tear film break up time</b>
<b>kg</b>	<b>Kilogram</b>	<b>t.i.d</b>	<b>Three times a day</b>
<b>L</b>	<b>Lymphocyte</b>	<b>TLC</b>	<b>Total leukocyte count</b>
<b>M</b>	<b>Monocyte</b>	<b>%</b>	<b>Percent</b>
<b>mg</b>	<b>Milligram</b>	<b>&lt;</b>	<b>Less than</b>
<b>min</b>	<b>Minute</b>	<b>&gt;</b>	<b>Greater than</b>
<b>mm</b>	<b>Millimeter</b>	<b>≥</b>	<b>Greater than or equal to</b>
<b>N</b>	<b>Neutrophil</b>	<b>@</b>	<b>At the rate of</b>
<b>ND</b>	<b>Non descript</b>	<b>VPR</b>	<b>Visual postural reflex</b>



**CHAPTER – 1**  
**INTRODUCTION**

## CHAPTER I

### INTRODUCTION

Kerato-conjunctivitis sicca (KCS) or dry eye syndrome is a frequently occurring canine ophthalmic multifactorial disease, resulting from inflammation of the cornea and conjunctiva or deficiency of one or more elements in the precorneal tear film (Berdoulay *et al.*, 2005, Williams, 2018). KCS is categorized into two types viz quantitative KCS and qualitative KCS as per the tear film deficiency where quantitative KCS causes a decrease in the aqueous component of the tear film and qualitative KCS results in a decrease in the lipid or mucin components of the tear film (Helper, 1996).

The precorneal tear film is crucial for preserving the ocular surface health, to provide the avascular cornea with nutrition (oxygen, glucose, electrolytes), lubricating the eye lids and ocular surface, providing protective antimicrobial proteins, immunoglobulins, growth factors, and to remove the debris and exfoliated cells (Dodi *et al.*, 2009).

Lacrimal gland secretion is controlled by the parasympathetic and sympathetic nervous system, hormones and various proteins i.e. epidermal growth factors. These layers are intricately intermingled over the corneal and conjunctival surfaces (Gipson *et al.*, 1992). The reduction in tear production causes corneal inflammation and in severe cases, cause permanent blindness.

The etiology of KCS includes, congenital (Herrera *et al.*, 2007), metabolic, infectious, drug induced (Berger *et al.*, 1995), neurogenic (Matheis *et al.*, 2012), radiation, iatrogenic (Saito and Kotani, 2001), idiopathic and immune mediated. Immune mediated form is found to be the most common type of KCS in dogs (Giuliano and Moore, 2007).

The pathological changes observed in KCS include compensatory conjunctival cell hyperplasia and increased mucin production because of reduction in the aqueous portion of tear film. In acute phase, the tear film becomes more hypertonic, leading to dehydration of the ocular surface epithelium, resulting in edema, vacuolar degeneration

and thinning of corneal conjunctival epithelium. Corneal epithelium is readily exfoliated by greater friction associated with blinking over a roughened, keratinized conjunctival epithelium and results into corneal ulcerations which are prone to infection, keratomalacia and perforation. Chronic surface irritation makes conjunctiva hyperemic and chemotic and the epithelium undergoes squamous metaplasia and hyperkeratinisation (Wilcock, 2008). The corneal epithelium also thickens and keratinizes which results in an irregular epithelial surface which may reduce the adhesion of the remaining tear film to the ocular surface. Inflammatory cells and blood vessels infiltrate the anterior corneal stroma and pigment, lipid, calcium may be secondarily deposited on the cornea. The vascularization and deposits stabilizes the cornea and make it less susceptible to ulcerations, however, the presence of inflammatory debris can result in loss of vision, corneal melting and perforation. The loss of antimicrobial substance suspended in the aqueous portion of tear film predisposes the dry eye to secondary bacterial infection (Cher, 2003).

Brachycephalic breeds of dogs (i.e., Pugs, American Cocker Spaniel, Lhasa Apso, Shih Tzus, Bull Mastiffs, English Bull dog, Boston Terriers, Blood Hounds etc.) are more susceptible to KCS (Kaswan and Salisbury, 1990) whereas, females of West Highland White Terriers are more likely to be affected with KCS (Sanchez *et al.*, 2007). It is more frequent in older animals than in younger ones.

KCS in dogs during the acute phase of disease is categorized by conjunctival hyperemia, blepharospasm, mucoid to mucopurulent ocular discharge. As the disease becomes chronic, KCS manifests corneal vascularization, fibrosis, pigmentation and corneal ulcerations (Berdoulay *et al.*, 2005). Tear film deficiencies can lead to chronic inflammation of ocular surface resulting in secondary infection and making eye more prone to ulcerations.

The diagnosis of KCS is based on the history (drug administration, cherry eye excision, repeated bouts of conjunctivitis that recur when topical medication is discontinued), presence of consistent clinical signs, measurement of decreased aqueous tear production by Schirmer tear test (STT I and STT II), tear film breakup time

(TFBUT) for evaluation of precorneal tear film stability using Fluorescein dye, Rose bengal stain test, eye lid margin examination and conjunctival biopsy (Williams, 2005).

Medical therapy aims to eliminate the cause when possible, to reactivate the tear film, stimulate the tears, control and prevent secondary bacterial infections and reduce the inflammation. Treatment includes administration of ocular tear stimulants, artificial tear solutions, broad spectrum ophthalmic antibiotics, anti-inflammatory agents and mucolytics (Matsuda and Koyasu, 2000). Surgical management of KCS can be considered when no response of medical therapy is observed which involves punctal occlusion, permanent partial tarsorrhaphy and parotid duct transposition (PDT) (Matsuda and Koyasu, 2000).

Cyclosporine is the first immunosuppressant to have a selective effect on lymphoid or T-cells and has the ability to block the transcription of cytokine genes in activated T-cells. Administering cyclosporine will stop the aggression of the lachrymal gland, decrease inflammatory process evidently diminishing corneal and conjunctival lesions, restore eye lubrication and enhance mucin production from conjunctival goblet cells (Schreiber and Crabtree, 1992 and Matsuda and Koyasu, 2000). The drug can be administered topically as a 0.2% ointment or as a 1% or 2% oil-based solution (Gilger and Allen, 1998).

Parotid Duct Transposition (PDT) has been observed to be a suitable surgical technique in KCS affected dogs. It involves freeing the parotid duct and papilla from the oral mucosa, mobilization and its transposition to the inferior cul-de-sac (Giuliano and Moore, 2007). PDT is a successful procedure which improves the ocular vision in medically refractive cases of KCS with minimal complications (Rhodes *et al.*, 2012; Schilke and Sapienza, 2012; Williams, 2018).

The study was therefore contemplated to be undertaken with the following broad objectives:

1. To study the prevalence of Kerato- conjunctivitis sicca in dogs.
2. To evaluate the efficacy of cyclosporine medication and surgical management by parotid duct transposition in the treatment of KCS in dogs.



**CHAPTER – 2**  
**REVIEW OF**  
**LITERATURE**

### REVIEW OF LITERATURE

Kerato-conjunctivitis sicca is a common condition of canine patients in veterinary practice and gaining importance as a leading cause of blindness. However, its diagnosis is frequently overlooked. Tear abnormalities are a leading cause of canine ocular surface disease, wherein the changes occurring in ocular surface health might lead to disease in the eye (Gelatt, 2000) resulting in reduced or loss of vision. This is a disease that requires life-long therapy, good client education and life-long monitoring. A brief review of literature related to the present study has been described below under the following headings:

- 2.1 Anatomy of lacrimal and salivary gland
- 2.2 Physiology and importance of tear film
- 2.3 Kerato-conjunctivitis sicca (KCS)
- 2.4 Incidence of KCS
- 2.5 Signalment
- 2.6 Etiology
- 2.7 Pathogenesis
- 2.8 Clinical signs
- 2.9 Diagnosis
- 2.10 Haemato-biochemical evaluation
- 2.11 Treatment
- 2.12 Post-treatment complications

#### **2.1 Anatomy of lacrimal and salivary gland**

Dugan *et al.* (1992) reported that lacrimal gland is small structure and is located more laterally at the medial surface of the orbital ligament and observed no significant difference in weight of gland on both sides but thickness of lacrimal gland is asymmetrical which could be an important indicator of unilateral disease.

Miller *et al.* (2008) observed that parotid gland is V in shape and lacrimal gland is flattened due to the location between bony orbit and eyeball and is responsible for production of lacrimal fluid. The parotid duct is approximately 1.5 mm in diameter and 6 cm long in medium breed mesaticephalic dogs (Sakai, 1989).

Eubanks and Woodruff (2010) observed that parotid gland is surrounded by horizontal ear canal. The margins of gland are indistinct because the gland is not surrounded by capsule as it blends with subcutaneous fat and connective tissue of the muscles of external ear parotid duct travels rostrally over the aponeurosis of masseter muscle and opens into the mouth on a prominent papillae at the level of maxillary fourth premolar teeth.

Evans *et al.* (2013) opined that dog's lacrimal gland is tubuloacinar gland on the episclera in the superior temporal orbit which produces approximately 60% of the serous portion of the tears.

## **2.2 Physiology and importance of tear film**

Carrington *et al.* (1989) observed that the tear film is trilaminar structure with a deep layer of mucins attached to the superficial epithelium, a middle or major layer of aqueous tears and a superficial layer of lipid which prevents aqueous tear evaporation. The aqueous tears is produced, by the lacrimal gland and the nictating gland, excising the gland has shown significantly higher proportion of cases of KCS to occur because 30% of aqueous tear production rises from the nictitans gland (Helper, 1970) and decrease in tear production, corneal inflammation may result in permanent blindness in very severe cases (Aguirre *et al.* 1971).

Grahn and Storey (2004) stated that precorneal tear film is a complex trilaminar fluid measuring approximately 7 to 10  $\mu\text{m}$ , whose main function is to correct corneal surface irregularities, in addition to promoting tear adhesion to the corneal epithelium.

Dodi *et al.* (2009) reported that the tears play an important role in maintaining the health and normal function of the cornea and conjunctiva. Tears provide lubrication and nutrition to cornea and help in flushing debris from the corneal surface. Tears contain

growth factors, immunoglobulins, lysozymes which act as ocular defense mechanism with antibacterial action.

Hirayama *et al.* (2013) reported that lacrimal fluid components helps to maintain the cornea by spreading a major source of proteins and electrolytes which act as nutrients and lubricates the bulbar and palpebral conjunctiva.

### **2.3 Kerato-conjunctivitis sicca (KCS)**

Kerato-conjunctivitis sicca is a chronic ocular disease characterized by inadequate secretion or excessive evaporation of tear film which ultimately leads to damage to the corneal and conjunctival surfaces and vision loss (Barabino *et al.*, 2004).

Stern *et al.* (2004) reported that dry eye condition is due to a chronic inflammation of the lacrimal functional unit, causing tear film dysfunction leading to alteration of tear aqueous, mucin and lipid components.

Zeev *et al.* (2014) stated that dry eye is one of the most commonly encountered problems in veterinary ophthalmology which includes low tear lakes, punctate epithelial erosions, hyperemia, rapid tear break up time and meibomian gland disease.

Conrady *et al.* (2016) reported that a loss or reduction in any layer of this film result in blurry vision and burning pain in eyes know as dry eye.

Williams (2018) observed that dry eye is a significant problem in both dogs and people, thus providing the best opportunity for translational medicine where advances in diagnosis and treatment can be translated to each other and providing spontaneous modes for human diseases.

### **2.4 Incidence of KCS**

Kaswan and Salisbury (1990) reported that kerato-conjunctivitis sicca is a common canine eye disease with an annual incidence of 0.3% to 1.52%.

Helper (1996) observed that 0.4% of the dogs are affected with the deficiency in tear production, Whereas, high prevalence of KCS has been reported by Kaswan *et al.*

(1985) and Ramani *et al.* (2017) to the extent of 35% and 52.50%, respectively in their various studies, where pugs (97.58%) were the most commonly affected breed.

Pal *et al.* (2008) has reported that dry eye is a chronic inflammatory disease with an incidence ranging from 11 to 14.7%.

## **2.5 Signalment**

Barnett and Sansom (1987) and Kaswan and Salisbury (1990) observed that brachycephalic dog breeds (Pugs, Lhasa Apso, Shih Tzus, Bull Mastiffs, English Bull dog etc.) are more prone to primary KCS. A study by Herrera *et al.* (2007) and Dodi (2015) have observed that the world wide recognized breeds predisposed to KCS are Cavalier King Charles Spaniels, English Bulldog, Lasa Apsos, Shih Tzu, West Highland White Terriers, Pugs, Blood Hounds, American Cocker Spaniels, English cocker Spaniels, English Springer Spaniels, Pekingeses, Boston Terriers, Miniature Schnauzers and Samoyeds, Yorkshire Terriers, Bedlington Terriers, English Cocker Spaniel. In Cavalier King Charles Spaniels dogs, KCS is associated with ichthyosiformdermatosis (dry eye curly coat syndrome).

Bron *et al.* (2003) stated that the dry eye condition is more common in older animals with the disease being more frequent in females than in males. However according to a study by Balicki *et al.* (2008), tear production decreases with age and higher incidence is seen in middle to old aged male dogs.

Matheis *et al.* (2012) observed that middle aged female dogs affected with neurogenic KCS showed dryness and crusting of the ipsilateral nares.

Amol (2016) reported the highest incidence of ocular affections in brachycephalic breeds of dogs in which 88% of pugs were highly affected with over all predominance of males 64%.

## **2.6 Etiology**

Barnett and Sasmon (1985) observed that palpebral ectropion and lagophthalmos increases the evaporation of tears and facilitates the uprising of KCS.

Kaswan *et al.* (1985) observed that dry eye symptoms are a result of infiltration of inflammatory cells. The normal inflammatory cell population of nictating membrane and lacrimal gland are 44% and 56% respectively and idiopathic canine KCS is indeed a T-cell predominanting immune-mediated or a autoimmune disease.

Berger *et al.* (1995) observed that the long term application of topical atropine and systemic sulphonamides, both resulted in reduced tear production and their effects could be either temporary or permanent. Dogs weighing less than 12 kgs undergoing treatment with oral trimethoprim-sulfadiazine were significantly at a greater risk of developing KCS.

Moore (1999) also reported similar results and stated that immune mediated is the primarily accepted cause of KCS which is generally bilateral and the result of immune-mediated inflammation and destruction of the lacrimal glands.

Saito and Kotani (2001) reported that iatrogenic KCS results because of the surgical removal of the third eye lid gland in case of cherry eye which is responsible for 30% of the tear production and 70% by the main orbital lacrimal gland. Failure of surgically corrected prolapsed third eyelid gland can lead to glandular scarring, atrophy and KCS.

Cullen *et al.* (2005) opined that diabetic cataractous dogs have altered precorneal tear film, which leads metabolic KCS.

De Almeida *et al.* (2009) reported that canine distemper virus, toxoplasmosis, leishmaniosis and chronic blepharoconjunctivitis can cause infectious KCS. Whereas, several known causes of KCS in dogs, including congenital, metabolic, infectious, drug induced, neurogenic, radiation, iatrogenic, idiopathic and immune mediated have also been reported by Dodi (2015).

Matheis *et al.* (2012) observed that a primary loss of parasympathetic innervation to the lacrimal gland (CN VII) or loss of sensory innervation to the cornea (CN V) leads to neurogenic KCS and neurological dysfunction as also reported by Kaswan *et al.*

(1985). These cases may have a history of orbital traumatic or inflammatory disease because the parasympathetic branch of the facial nerve innervates the lateral nasal glands.

## **2.7 Pathogenesis**

Jabs *et al.* (2001) reported that CD4+ T release cytokines that contribute to development of KCS. Additionally, apoptotic mediators like as p53, fas, and fasL were highly expressed in ocular surface that play a role of apoptosis in association with immune mediated inflammation in the pathophysiology of dry eye (Gao *et al.*, 1998).

Kunert *et al.* (2002) observed that KCS revealed high number of CD4+ T cells in conjunctival inflammation. Infiltration of inflammatory cells, predominantly T lymphocytes resulted in squamous metaplasia, where the conjunctiva becomes a keratinized stratified squamous epithelium, accompanied by epithelial stratification, metaplasia of superficial epithelial cells and loss of goblet cells.

Stern *et al.* (2004) observed that the dry eye condition results from a systemic autoimmune to a local autoimmune event, due to lack of systemic androgen support to lacrimal gland and factors such as neurogenic inflammation and T-cell involvement facilitate the factors in the initiation of this pathophysiology.

## **2.8 Clinical signs**

Salisbury *et al.* (1995) observed that redness signals kerato-conjunctivitis with a mucoid to muco-purulent ocular discharge. Conjunctival redness involves the conjunctiva of both the globe and the eye lid, while intraocular inflammation or uveitis gives a hyperaemia of the episclera and limbus known as ciliary flush which comes from cytokines percolating through the sclera and episclera from the ciliary body.

Marsh and Pflugfelder (1999) reported that the ocular lesions presented in KCS are related to the lacrimal deficiency and immune-mediated inflammation affects either lacrimal gland or the ocular surface and shows signs of conjunctival hyperemia, ocular irritation, chemosis, blepharospasm and photophobia (Kunert *et al.*, 2002).

Berdoulay *et al.* (2005) observed that the clinical signs of KCS vary according to gravity and onset of the illness. During the acute phase of disease, conjunctiva is extremely reddish with dense yellow or greyish discharge and ocular surface is less bright. In the chronic phase, eye manifests corneal vascularization, fibrosis, pigmentation, recurrent corneal ulceration, blindness or even loss of the eye.

Williams and Hewitt (2017) stated that a normal uninterrupted tear film over the corneal surface gives a crystal clean reflection but canines affected with KCS have a dull lustreless ocular surface when a reflection of penlight is directed at cornea and does not have sharp boundary, but rather is broken up into many small individual reflections.

## **2.9 Diagnosis**

Barnett and Sasmon (1985) observed that diagnosis is made on the type, quantity and position of the typical discharge which is easy, to identify by the schirmer tear test or the use of 1% rose bengal. Rose bengal stains conjunctival cells and mucus a bright rose red when they are devitalized by drying. Complete haematological and serum chemistry profile and cultures are needed to rule out bacterial infections should be considered.

Lewin (2014) reported that the diagnosis of KCS depends first and foremost on consideration of the signalment, history and clinical findings and any patient presented with any ocular complaint should have their tear production measured with a schirmer tear test.

### **2.9.1 Neuro-ophthalmic examination**

Moore (2001) suggested that pupillary light reflex is a test to evaluate the integrity of the sensory and motor functions of the eye.

Turner (2008) reported that menace response is to be used to assess the visual pathway and eyelid function. False positive response is caused due to air currents generated. A negative menace response usually indicates blindness, although animals with cerebellar lesions and normal vision may also have a negative menace response (Mitchell, 2011).

Thompson *et al.* (2010) reported that knowledge of the neuroanatomical pathway for pupillary light reflex helps in pin pointing the location of lesion and also mentioned that pupillary light reflex response was not an assessment of vision as blind animals can have normal PLRs (e.g., those with cataracts or occipital cortex lesions) and those with normal vision can have absent PLRs (e.g., animals with iris atrophy).

Mitchell (2011) discussed that the dazzle reflex was used to check the potential vision in cases with some opacity of the ocular media in which a bright focal light source was shone quickly into the eye and resulted in closure of the eyelids and, to a lesser extent the contralateral eyelids. A negative dazzle is a poor prognostic indicator for vision.

Featherstone and Heinrich (2013) reported that the palpebral reflex was elicited by lightly touching the periocular skin at the medial and lateral canthus which resulted in closure of the eyelids. A normal result confirms an intact sensory (trigeminal nerve) and motor pathways (facial nerve). An abnormal result (lack of a blink) indicates poor sensation or a facial nerve paralysis.

### **2.9.2 Schirmer tear test**

Schirmer (1903) carried out a clinical study on the physiology and pathology of tear secretion and its removal and reported that Schirmer tear test I whereas, Schirmer tear test II is performed after the application of topical local anesthetic which measures the basal tear production alone.

Moore *et al.* (1987) studied twenty-four healthy young adult laboratory beagle dogs between the age of 9-18 months and recorded the mean Schirmer tear test (STT-I) values of  $23.42 \pm \text{SD } 6.25$  and  $24.29 \pm \text{SD } 5.58$  mm/min for left and right eyes with no significant difference in STT values among male and female dogs.

Hollingsworth *et al.* (1992) conducted a study on the effect of topically administered atropine on tear production in dogs and reported an altered STT value and temporary dryness for 2-6 days. Transient decrease in tear production after topical

administration of atropine which indicated atropine becomes more pronounced over time was marked at 120 min and returned to base line value by 300 min of installation.

Berger and King (1998) studied fluctuation in tear production in canines and observed significant differences in both STT I and STT II values in dogs which indicated that weight has significant effect on STT values. Larger dogs have higher basal tear production compared to dogs with lesser body weight. He also reported fluctuations in the STT values on both daily and weekly basis which were biologically significant on a week to week basis.

Hamor *et al.* (2000) reported that the standard tear production in dogs is >15 mm/min, values between 10mm/min and 15mm/min are doubtful, while dogs with values between 5mm/min and 10mm/min are suspicious and STT <5mm/min is diagnosed as KCS. However, Hendrix *et al.* (2011) have observed that the dogs with KCS have a STT of <10mm/min and severely affected dogs often have a STT result of 0mm/min.

Herring *et al.* (2000) reported that Schirmer tear test is the cornerstone of quantitative KCS in dogs where the normal production is >15mm/min. STT is measured by placing sterile test paper in the lower conjunctival fornix, after folding the strip of filter paper (35mmx5mm) at the notch and putting the folded portion between the cornea and lower lid for one minute and thereafter recording the length of wetting of the strip.

Williams (2005) analyzed the uptake of tears in Schirmer tear test (STT) both invitro and invivo in 100 ophthalmologically normal dogs together with a group of 40 dogs with KCS. In his study he concluded that temporal examination of STT allowed a more precise evaluation of tear production than the standard STT measuring tear uptake in 1 min, along with estimation of residual tear lake volume and those from continual tear production.

STT is a semiquantitative method for measuring production of the aqueous portion of the precorneal tear film, canine eye (Maggs, 2008).

### 2.9.3 Tear film break up time (TFBUT)

The tear film breakup time (TFBUT) is a test for evaluation of lipid and mucin deficiencies in the tear film using the sodium fluorescein dye and the time is taken for the appearance of dark or dry spots on cornea after application of the dye with eyelids held open and recorded in seconds (Davidson and Kunonen, 2004).

Moore and Collier (1990) stated that ocular surface disease is associated with loss of conjunctival goblet cells in dogs and revealed a marked reduction in number of goblet cells under Periodic Acid Schiff staining and concluded that the animals with quantitative deficiencies often have a TFBUT of < 5 seconds which indicate an unstable precorneal tear film where as normal TFBUT is > 20 seconds.

Saito and Kotani (2001) reported that the normal mean value of tear film breakup time in normal Beagle dogs is  $21.53 \pm \text{SD } 7.42$  seconds.

Cullen *et al.* (2005) described TFBUT as a test which measured the precorneal tear film stability and was used to support a presumptive diagnosis of qualitative tear film dysfunction. The tear film breakup time (TFBUT) values were compared among diabetic cataractous, non-diabetic cataractous and non-diabetic dogs and reported the mean value of TFBUTs were significantly lower ( $6.6 \pm 3.8\text{s}$ ) in diabetic cataractous dogs. Rapid TFBUTs of 2 to 5 sec was documented in dogs with mucin deficiency, associated with ulcerative and non-ulcerative keratoconjunctivites.

Giuliano and Moore (2007) studied that the fluorescein dye is essential to assess the tear film break up time (TFBUT) which is normally 15 to 25 seconds, whereas a value of 10 seconds or less is indicative of qualitative tear film instability, where as ophthalmic Rose Bengal dye has been observed to be a vital stain because of its ability to stain the nuclei of cells by Doughty (2013).

Nagaraj, (2011) has observed  $8.75 \pm 0.39$  seconds value of tear film breakup time (TFBUT) in 52 dogs affected with KCS.

Williams and Hewitt (2017) stated the key feature assessed by the TFBUT is the removal of tears by evaporation and nasolacrimal drainage. In brachycephalic breeds

there is significantly increase in evaporative loss of tears from the central corneal surface and thus an evaporative dry eye. Breeds such as pugs and Pekingese have high prevalence of ocular surface pigmentation because of excessive loss of fluid from the central tear film which is a significant factor in development of these pigmentary changes. TFBUT is determined by using fluorescein dye which may alter the physiology of the ocular surface.

#### **2.9.4 Microbiological examination**

Whitley (2000) reported the efficacy of ciprofloxacin, norfloxacin, and ofloxacin as topical ophthalmic antibiotics in the management of ocular bacterial infections. Bacterial infections are usually associated with diseases of the eyelids, cornea and conjunctiva due to loss of antimicrobial properties in tear film.

Gelatt *et al.* (1985) observed that gentamicin was the most sensitive antibiotic for treatment of ophthalmic infections in dogs.

Bharathi (2009) conducted study on seven cases of conjunctivitis, in which *staphylococcus* spp. in six cases and *klebsiella* spp. in one case was found to be the causative organism. Ciprofloxacin was the antibiotic of choice as per culture and antibiotic sensitivity tests, followed by cefotaxim, ceftriaxone and gentamicin.

Williams *et al.* (2012) observed that the ocular discharge seen in KCS suggests that bacterial infection is responsible for ocular signs. Eyes with deficient tear production are no more infected with bacteria than are eyes with normal tear production.

Ramani *et al.* (2013) performed the antibiotic sensitivity test for corneal culture isolates from dogs and revealed that the pathogens were more sensitive to cefotaxime (68%), tetracycline (47%), gentamicin (36%), azithromycin (26%) and amoxicillin (21%).

#### **2.10 Haemato-biochemical evaluation**

Stevenson *et al.* (2000) conducted a study to document that the mean  $\pm$ SE values of physiological, haematological and serum biochemical parameters do not show any

significant variation except for eosinophil count. Eosinophil values were significantly higher in group in which cyclosporine 0.05% was used as treatment regime.

Hendrix *et al.* (2011) reported that the serum biochemistries were within normal range after application of topical ocular tacrolimus and cyclosporine in dogs.

Williams (2010) observed that there was no change in lymphocyte stimulation index nor were significant blood levels of cyclosporine documented after topical administration of 0.2% or 2% cyclosporine.

Nagaraj (2011) reported a mean  $\pm$  SEM total erythrocyte count (TEC) and total leukocyte count (TLC) values of  $6.82 \pm 0.13$  million/ $\mu$ l and  $9608.65 \pm 199.6$  thousands/ $\mu$ l, respectively in 52 dogs affected with KCS.

## **2.11 Treatment**

Various treatment regime for KCS have been tried and recommended by various researchers are listed below.

### **2.11.1 Medicinal treatment**

Barnett and Sansom (1985) advised treatment of Kerato-conjunctivitis sicca (KCS) with artificial tears, lacrimogenics, antibiotics, corticosteroids, mucolytics and hormones.

Kaswan and Salisbury (1990) reported that 80% of dogs regained normal levels of tear production using treatment with cyclosporine and observed improvement in STT value from 2mm/min to 14mm/min.

Morgan and Abrams (1991) reported that cyclosporine was evaluated was isolated from the fungus *Tolyposcladium inflatum* in 1976, which is a lipophilic, neutral cyclic undercapeptide and is the first immunosuppressant to have a selective effect on lymphoid or T-cells. Topical administration of 2% cyclosporine was used for the treatment of KCS in 60 dogs. Where burning response to application of cyclosporine resolved with change in the formulation of topical solution and improvement in tear production and reduction of corneal pigmentation was seen in 75% and 67% of eyes, respectively.

Olivero *et al.* (1991) on using 1% cyclosporine topically in KCS affected dogs reported improvement of 100% and 81.8% in Schirmer tear wetting values and clinical signs, respectively.

Schreiber and Crabtree (1992) observed that administering cyclosporine will stop the aggression of the lachrymal gland, stop the inflammatory process evidently diminishing cornea and conjunctiva lesions, restore eye lubrication and enhance mucin production. The drug can be administered topically as a 0.2% ointment and as a 1% or 2% oil- based solution (Gilger and Allen, 1998).

Moore (1999) suggested 0.2% cyclosporine A (CsA) ointment for treatment of kerato-conjunctivitis sicca in 12 dogs where 24 eyes were evaluated. They observed improvement of tear production in dogs with STT values ranging from  $5.5 \pm 2.3$ mm/min to  $11.8 \pm 4.1$  mm/min for left eye and  $4.4 \pm 2.5$  mm/min to  $12 \pm 4.6$ mm/min for right eye with marked regression of chronic corneal neovascularization and granulation. According to them CsA also caused reduced conjunctivitis caused rapid healing of corneal ulcers and reduced dependence on other topical treatments.

Matsuda and Koyasu (2000) studied that the mechanism of action of cyclosporine as a potent immuno suppressive agent which had the ability to block the transcription of cytokine genes inactivated T-cells. They also observed that cyclosporine blocks the JNK (c- Jun N-terminal kinases) and p38 signaling pathways triggered by inhibiting T-cells proliferation antigen recognition, making cyclosporine A and highly specific inhibition of T-cell activation.

Gelatt (2000) advised treatment of eyelid diseases with administration of oral or parenteral antibacterials, antihistamines, topical triple antibiotic (neomycin, polymyxin B, and bacitracin) and 1% prednisolone or 0.1% dexamethasone ointment.

Berdoulay *et al.* (2005) investigated the effect of 0.02% tacrolimus in aqueous suspension on tear production in dogs with KCS where they reported that KCS is a chronic ophthalmic disease resulting from deficiency of one or more elements in precorneal tear film and concluded that 0.02% tacrolimus effectively increased tear production in dogs with KCS.

Behrens *et al.* (2006) reported that artificial tears provide palliative relief to eye irritation in canines with aqueous tear deficiency and also observed that combinations of artificial tears, oral omega-3 essential fatty acid supplements, mucin seretagogues, short term steroids and daily cyclosporine are used to combat underlying inflammation that restores normal tear film in patients with mild to moderate disease.

Utine *et al.* (2010) observed that cyclosporine exerts immunosuppressive, anti-inflammatory activity, increases tear secretion and tear film stability. Topical cyclosporine help in restoring epithelial damage and also reduces disease recurrences over the long term.

Hendrix *et al.* (2011) conducted a study on the administration of ophthalmic 2% cyclosporine and 0.03% tacrolimus in KCS affected dogs for 3 months and reported that both the drugs were equally efficacious in increasing the STT-I values.

Nagaraj (2011) observed that administration of cyclosporine eye drops @ 1 drop, q 12 hr, 2% pilocarpine eye drops @ 2 drops/ 10kbw, orally, s.i.d, 0.7% hydroxypropyl methylcellulose eye drops @ 1 drop, q 8 hr for 6 months and 0.3% ciprofloxacin eye drops @ 1 drop, q 8 hr for 1 month effectively treated dogs affected with KCS.

### **2.11.2 Surgical treatment**

Bennett (1968) were first researchers who described PDT as treatment for KCS in humans in 1950, and Lavignette, (1966), first reported the technique in canines in the year 1966.

Schmidt *et al.* (1970) conducted a study on parotid duct transposition and reported that the success rate for PDT ranges from 63% to 80% and reported complications like calcium deposition on eye lid margin, post-operative facial swelling, conjunctival hyperemia and continuous salivary epiphora.

Punctal duct occlusion and permanent partial tarsorrhaphy have shown limited usefulness in severe KCS cases (Williams, 2002) but PDT has been reported to be the most suitable choice in majority of cases (Giuliano and Moore, 2007).

Ozgenel *et al.* (2000) conducted a study on ten dogs by performing stensen's duct repositioning by obtaining anesthesia using ketamine hydrochloride 10-20mg/kg body weight, 2% xylazine hydrochloride (0.15ml/kg) and was maintained with ketamine hydrochloride 5mg/kg.

Scotti *et al.* (2007) conducted a study on five year old female with a surgical method of parotid duct transposition and reported that the parotid papilla can be catheterized by using 2/0 nylon suture or with a 24G intravenous cannula.

Schilke and Sapienza (2012) reported that a key technique for restoring ocular health is surgical transposition of the parotid salivary duct into the ventral conjunctival sac. Saliva and tears are both ultra filtrates of plasma and thus PDT is the ideal solution for dry eye.

Rhodes *et al.* (2012) performed parotid duct transposition (PDT) in 92 eyes of dogs to determine success (92%) and failure rate (8%) and concluded that PDT is a successful procedure based on clinical findings which improves the ocular comfort and vision in medically refractive cases of KCS. Similar results were also reported by Lewin (2014) and Dodi (2015) who observed that parotid duct transposition is most suitable surgical treatment to KCS affected dogs.

Yoon *et al.* (2016) observed that the atropine sulphate to be a potent anticholinergic and also recommended the use of propofol for safe induction and maintenance of anesthesia for ophthalmic surgery.

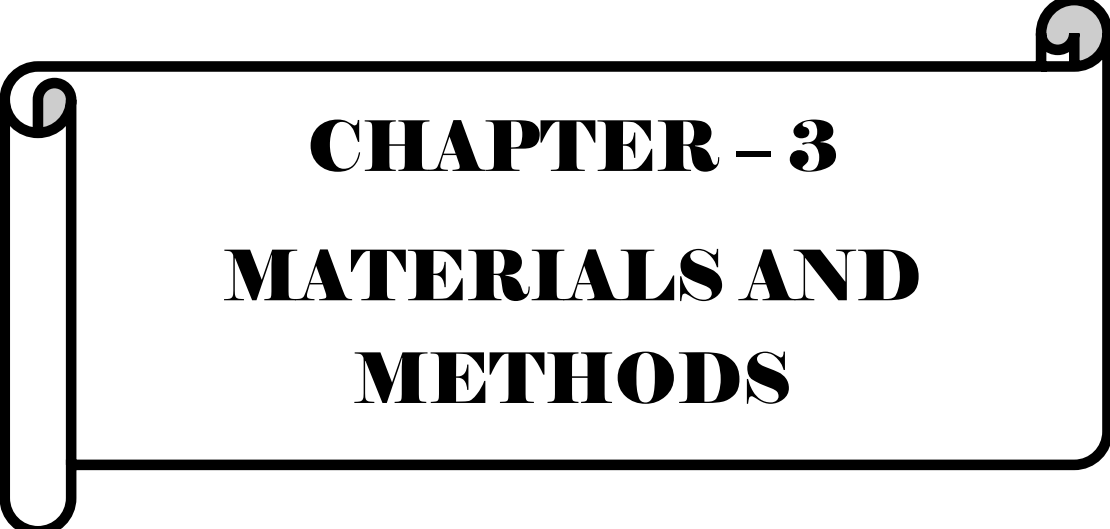
## **2.12 Post-treatment complications**

Morgan and Abrams (1991) reported that the disadvantages of cyclosporine are burning sensation to eyes, local irritation when used in more concentrated preparations and sometimes no improvement in corneal vascularization.

Mitchell (2011) observed that the complications associated with parotid duct transposition were failure of surgical technique due to twisting or stenosis of the parotid duct, sectioning of duct during dissection, corneal ulceration due to conjunctival sutures,

blepharitis, precipitation of calcium salts on the corneal surface and eye lid margins which cause irritation to patient.

Rhodes *et al.* (2012) and Williams (2018) reported that severe intolerance to saliva may lead to reversal or repositioning of parotid duct transposition. They also observed progressive corneal pigmentation which is common sequel to chronic corneal irritation in dog leading to reduced visual acuity.



**CHAPTER – 3**  
**MATERIALS AND**  
**METHODS**

### MATERIAL AND METHODS

#### 3.1 Technical programme

The study was conducted on ten dogs affected with kerato-conjunctivitis sicca (KCS) brought to the Teaching Veterinary Clinical Complex, F.V.Sc & A.H, R.S.Pura, Jammu, during the period from August 2018-June 2019. After recording the thorough history, all the dogs were subjected to a detailed ophthalmic examination and the following parameters were investigated and recorded on days 0, 15, 30 and 45.

##### 3.1.1 Signalment

Age, breed, sex and weight of the animal affected with KCS were recorded.

##### 3.1.2 Case history

Detailed history of each affected dog like chief complaint and symptoms noticed by the owner, any ocular discharge, presence of vision, cause and duration of damage, previous ocular disease, rapidity of progression, prior treatment before presentation and vaccination status, were recorded.

##### 3.1.3 General clinical examination

Clinical examination of each dog affected with KCS was performed and parameters like, rectal temperature ( $^{\circ}\text{F}$ ), heart rate (beats/min) and respiratory rate (breaths/min) were recorded before treatment and at regular intervals after treatment till day 45.

##### 3.1.4 Ophthalmic examination

Ophthalmic examination was conducted for all the ten dogs affected with kerato-conjunctivitis sicca.

###### 3.1.4.1 Gross examination

Both eyes and periocular regions were grossly examined by naked eye in day light and abnormalities, if any, were recorded. The eyes were examined for presence of photophobia, and conjunctival mucous membrane colour.

### **3.1.4.2 Neuro-ophthalmic Examination**

The following ophthalmic tests were performed in all the cases on the day of presentation day 0, 15, 30 and 45 day as described by Slatter (2001).

#### **3.1.4.2.1 Pupillary light reflex (PLR)**

The PLR was performed to evaluate the size of the pupils. For direct PLR, a focal light source was pointed in front of the nose of patient to assess the size of pupils and the resultant constriction of pupil was recorded. This was graded as: strong (+++), moderate (++) , mild (+) and absent (-) (Strubble, 1991)

Strong (+++): Complete and rapid constriction of the pupil seen during testing of both direct and consensual PLR.

Moderate (++) : Incomplete or slower constriction of the pupil

Mild (±): Very slow constriction of the pupil

Absent (-): No response of pupil to light

#### **3.1.4.2.2 Cotton ball test**

This test was performed to know the dog's ability to follow movements when a cotton ball was dropped about 6 inches away from the dog by covering one eye. Animal's response was judged by not only moving their eye but also sniffing (sometimes trying to eat) when the cotton ball lands. The reflex was graded as positive/sluggish/absent in response to stimulus as under:

Positive (+): Complete and consistent moving of eye

Sluggish (±): Incomplete/inconsistent moving of eye

Absent (-): No response shown by animal

#### **3.1.4.2.3 Dazzle reflex test**

This test was conducted by directing a strong light source on to the eye ball and observing it for partial or complete eyelid closure on the illuminated side.

Positive (+): Complete closure of eyelid/head retraction away from the source of light.

Sluggish ( $\pm$ ): Inconsistent closure of eyelids/head retraction.

Negative (-): No response shown by animal.

#### **3.1.4.2.4 Palpebral reflex**

Partial or complete closure of the eyelids in response to gentle tap with the tip of the finger or cotton bud at the lateral canthus of the eye or gentle stroking of the eyelashes in response to stimulus was graded as positive, sluggish or negative.

Positive (+): Complete and consistent closure of eyelids

Sluggish ( $\pm$ ): Incomplete or inconsistent closure of eyelids

Negative (-): No response shown by animal.

#### **3.1.4.2.5 Menace reflex test**

A menace response was evoked by making a sudden threatening gesture with the hand behind a transparent plexiglass without touching the patient at each eye while covering the other eye. Animal's response (blinking, head movement) was observed. The reflex was graded as positive/sluggish/absent in response to stimulus as under:

Positive (+): Complete and consistent closure of eyelid

Sluggish ( $\pm$ ): Incomplete/inconsistent closure of eyelids

Absent (-): No response shown by animal

#### **3.1.4.2.6 Visual placing postural reaction**

The animal was brought to a table edge and held off the ground. If the animal saw the table and elevated its limbs to place them on it was considered positive otherwise negative.

Positive (+): Dog was able to elevate its limbs and place them on the table.

Sluggish ( $\pm$ ): Delayed response to judge the table and place the limbs.

Negative (-): unable to detect the table.

### **3.1.5 Diagnostic test**

The following diagnostic tests were performed in all cases on the day of presentation day 0, 15, 30 and 45 day, as described by Slatter (2001).

#### **3.1.5.1 Schirmer tear test**

This test was done using sterile, individually packaged strips (Visioaid, Sava vet, Gujarat, India) before application of any topical solutions before treatment and after treatment at regular intervals. Animals were properly restrained and the Schirmer tear test (STT I) strip was folded at the notch and hooked over the middle to lateral third of the lower eyelid for one minute. The extent of strip wetting (mm/minute) was read immediately after removal from the eye and was compared to millimeter scale (Plate no 1).

The values were graded as:  $\geq 15$  mm/min = Normal production; 11–14 mm/min = Early or Subclinical or Mild KCS; 6–10 mm/min = Moderate KCS;  $\leq 5$  mm/min = Severe KCS and epiphora ( $>25$ mm/min) (Williams, 2005).

Schirmer tear test II was performed after application of topical local anaesthetic (0.5% Proparacaine hydrochloride) and then again strip was folded at the notch and hooked over the middle to lateral third of the lower eyelid for one minute. The extent of strip wetting (mm/minute) was read immediately after removal from the eye (Hartely *et al.*, 2006) (Plate no 2).

#### **3.1.5.2 Tear film break up time / Fluorescein staining test**

The fluorescein solution (Fluo strips, Contacare ophthalmic & diagnostic, Gujarat, India) was applied to the eye and the animal was allowed to blink with the eyelids held open until the tear film began to dissociate from the corneal surface. Dissociation resulted in the formation of a dry spot which appeared as a dark round area within the fluorescent tear film. The time (in seconds) was measured from the application of the stain up to

### Plate 1: Schirmer Tear Test- I



1a: Schirmer tear test strips used during the study

1b: STT strip is placed at lower eyelid for one minute

### Plate 2: Schirmer Tear Test- II



2a: Topical Local anesthetic 0.5% proparacaine hydrochloride used to perform STT-II

2b: STT strip hooked over the lower eyelid to measure the extent of strip wetting

### Plate 3: Tear Film Break Up Time (TFBUT)



3a: Fluorescein dye strips used during the study

3b: Heine Beta 200 (HEINE Optotechnik GmbH & Co. KG, Germany) used during the study



3c: Fluorescein dye installed on bulbar conjunctiva for TFBUT

3d: Observation of dry spot using cobalt blue filter of direct ophthalmoscope

dissociation of the spot. Observation was facilitated by using cobalt blue filter of the direct ophthalmoscope (Plate no 3).

### **3.1.6 Microbiological examination**

#### **3.1.6.1 Antibiotic Sensitivity Test (AST)**

AST was performed in all the cases. The conjunctival cultures were obtained prior to the administration of any topical solution. The eyelids were retracted and a sterile swab moistened with 0.9% normal saline solution (NSS) was passed back and forth on the affected area and was streaked on Mueller Hinton agar and antibiotic discs were placed on it. These agar plates were incubated for 24 hours at 37°C for bacterial growth (Plate no 4).

### **3.1.7 Haemato-biochemical estimation**

#### **3.1.7.1 Biochemical analysis**

Blood glucose (mg/dl), Serum albumin (g/dl), Serum globulin (g/dl) and Total protein (g/dl) were estimated in all cases on 0, 15, 30 and 45 day.

#### **3.1.7.2 Haematological estimations**

Venous blood sample was collected in ethylene diamine tetra acetate (EDTA) vial from the cephalic/saphenous vein and following tests were performed on the day of presentation: Haemoglobin (g/dl), Packed cell volume (%), TLC ( $\times 10^3 \mu\text{l}$ ), DLC (%) as per method described by Jain (1986).

## **3.2 Management of KCS**

The present clinical study was conducted on ten dogs of either sex, aging seven months to 10 years and weighing 5 kg to 42.3 kgs, presented to Teaching Veterinary Clinical Complex, F.V.Sc. & A.H., R.S. Pura, Jammu for kerato-conjunctivitis sicca over a period of one year. The ophthalmic examination was performed in all the dogs either with or without chemical restraint. The cases of KCS were randomly divided into two treatment groups of five dogs each (Table 3).

**Table 3.1 Design of work**

<b>Groups</b>	<b>Treatment</b>	<b>No. of cases (n)</b>
I	Medicinal treatment: Cyclosporine ophthalmic ointment (2mg/gm)	5
II	Surgical treatment: Parotid duct transposition (PDT)	5

Group I dogs were by topical application of cyclosporine ophthalmic ointment<sup>1</sup> (2mg/gm) b.i.d for 45 days, flurbiprofen<sup>2</sup> eye drops, methylcellulose<sup>3</sup> eye drops q.i.d, Gatifloxacin<sup>4</sup>/ Moxifloxacin<sup>5</sup> drops t.i.d for 2 weeks. (Plate no 5)

Group II dogs were treated surgically using parotid duct transposition technique (PDT) as described by Slatter (2001). All surgical manipulations were done under atropine, xylazine hydrochloride, ketamine hydrochloride and diazepam anaesthesia. The dogs were pre-medicated with inj. atropine sulphate<sup>6</sup> @ 0.04 mg/kg b.wt. i.m, followed 20 minutes later by inj. xylazine hydrochloride<sup>7</sup> @ 2 mg/kg b.wt. i.m, and ketamine hydrochloride administration<sup>8</sup> @ 10 mg/kg b.wt. i.m five minutes after xylazine HCL administration. The anesthesia was maintained by incremental doses of a mixture of diazepam<sup>9</sup> @ 0.14 mg/kg b.wt. and ketamine HCl @ 3.5mg/kg b.wt (1:25w/w) as and when required. Intravenous line was maintained by using normal saline solution<sup>10</sup> (0.9%). Inj. ceftriaxone<sup>11</sup> @ 25 mg/kg b.wt and inj. meloxicam<sup>12</sup> @ 0.3 mg/kg b.wt were administered intravenously pre-operatively in all the five dogs of group II.

<sup>1</sup> Visiocare (Savavet, Gujarat India)

<sup>2</sup> Flur ophthalmic drops (Allergan India Pvt. Ltd., India)

<sup>3</sup> Takfresh eye drops (Pharntak ophthalmics Pvt. Ltd., India)

<sup>4</sup> GFC eye drops (Pharntak ophthalmics Pvt. Ltd., India)

<sup>5</sup> Moxitak eye drops (Pharntak ophthalmics Pvt. Ltd., India)

<sup>6</sup> Tropine (Neon laboratories Ltd., India)

<sup>7</sup> Xylaxin (20mg/ml) (Indian Immunologicals Ltd., India)

<sup>8</sup> Aneket (50mg/ml) (Neon laboratories Ltd., India)

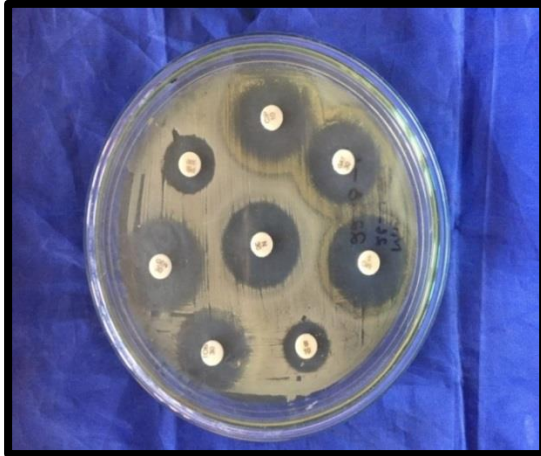
<sup>9</sup> Lori (5mg/ml) (Neon laboratories Ltd., India)

<sup>10</sup> NSS (PFL Pvt. Ltd., India)

<sup>11</sup> Monocef (Aristo pharma. Pvt. Ltd., India)

<sup>12</sup> Melonex (5mg/ml) (Intas pharmaceuticals, Ahmedabad, India)

### Plate 4: Antibiotic Sensitivity Test



4a: Antibiogram pattern of seven antibiotics by disc diffusion on Mueller Hinton agar

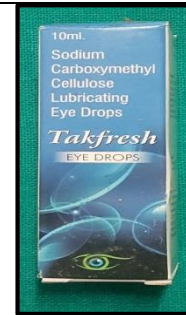
### Plate 5: Medicinal Treatment (Group-I): Topical Ocular Medications used



5a: Cyclosporine ophthalmic ointment (2mg/gm) used in group-I



5b: Antibiotic drops used post-treatment in group-I and II



5c: Artificial tears used in this study

The dog was restrained in lateral recumbency with the affected side upwards. The surgical treatment was carried out in five cases by preparing the lateral surface of face of the affected side for the surgery, the parotid papilla was cannulated with 24 gauge intravenous catheter<sup>13</sup> for identification and manipulation of the duct. Povidone iodine solution<sup>14</sup> was used as topical germicidal. The skin incision was given on lateral aspect of the face, the papilla and duct were dissected free from the labial mucosa just above the upper 4<sup>th</sup> premolar to the point where the duct detaches from the gland. From there a subcutaneous tunnel was made by blunt dissection to the inferior-lateral conjunctival cul-de-sac, where papilla was sutured in place by using 6/0 polygalactin<sup>15</sup> suture and skin sutures were closed by using nylon sutures. (Plate no 6)

### **3.3 Post – operative treatment**

Elizabethan collar was used in surgical treated cases to prevent self mutilation until a regular supply of parotid duct secretions was established. Cyclosporine ophthalmic ointment b.i.d for 45 days of observation period, methylcellulose eye drops q.i.d, flurbiprofen drops t.i.d. Gatifloxacin/ Moxifloxacin drops t.i.d., were used for two weeks only and discontinued later on. Small, regular amounts of food and soft food was recommended to be given to establish a continuous supply of secretions until skin sutures were removed on 10<sup>th</sup> day. The owner were asked to monitor the patient for changes in demeanour, pawing/ rubbing at the face. Any changes, if recorded, were reported.

### **3.4 Post – operative outcome, complications and their management**

Improvement in ocular health of all the cases was done by re-evaluating at every fifteen day interval up to 45 day by recording the changes in the clinical signs and by various other test. Outcome of the treatment, including complications, if any, and their management were also observed. Any improvement in dry eye as compared to the preoperative condition of the patient was noted and improvement percentage [(Increase ÷ Day 0 reading) × 100) was calculated.

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<sup>13</sup> Neocath (Romsons scientific and surgicals, Agra, India)

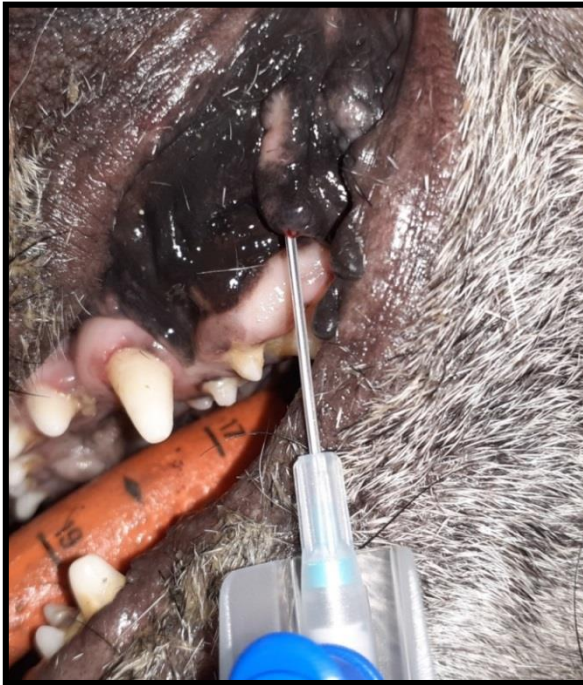
<sup>14</sup> Betadine topical solution (Win medicare pvt. Ltd., India)

<sup>15</sup> Sterilon, (Stericat Gutstrings (P) Ltd., Gurgaon, India)

### **3.5 Statistical analysis**

The data generated was statistically analyzed using student 't' test at 5% level of significance, and ANOVA using SPSS 16.0 computer software.

**Plate 6: Surgical treatment: Parotid Duct Transposition (Group-II)**



6a: Parotid papilla catheterization using 24G intravenous catheter



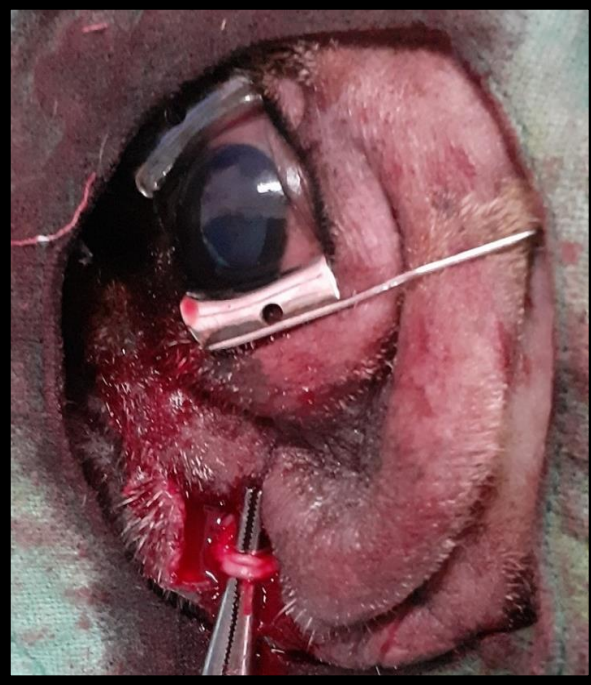
6b: Suture in place at parotid papilla to prevent it from becoming dislodged during dissection



6c: Draping the lateral surface of cheek of the affected side



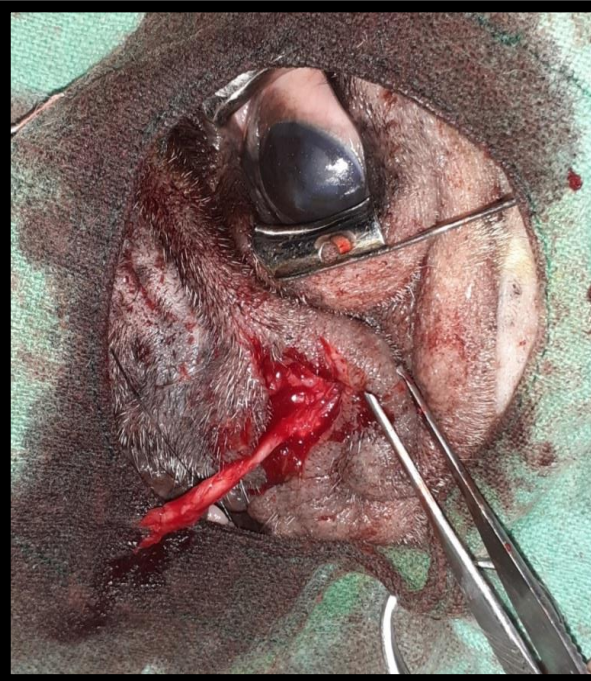
6d: Skin incision on the cheek area



6e: Isolation of parotid duct from the masseter muscle and surrounding tissue



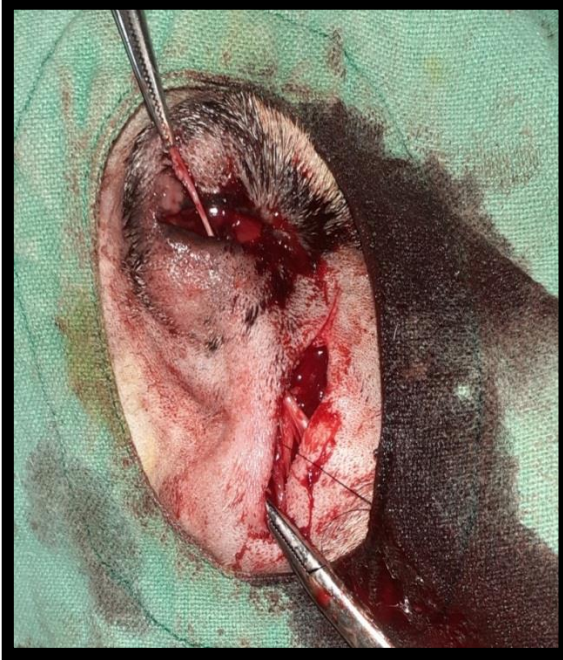
6f: Arrow showing base of parotid gland



6g: Blunt Dissection used to separate parotid duct



6h: Mosquito forceps used to make subcutaneous tunnel into ventral conjunctival sac



6i: Positioning of parotid duct into the conjunctival sac



6j: Parotid duct sutured using 6/0 polygalactin sutures



6k: Closure of facial entry using nylon suture



6l: Elizabethan collar applied after surgery



**CHAPTER - 4**  
**RESULTS**

### RESULTS

The study was conducted on dogs brought to the Teaching Veterinary Clinic Complex, F.V.Sc. & A.H, R.S. Pura, Jammu, during the period from August 2018 – June 2019.

One thousand four hundred ninety eight (1498) dogs were presented to Teaching veterinary clinical complex in which seven hundred two cases were of canine cases among which sixty three (63) dogs were affected with ocular affections. During the study period, twenty two (22) dogs were detected with kerato-conjunctivitis sicca with or without associated ocular affections based on Schirmer tear test I, II and TFBUT. Ten (10) dogs affected with KCS alone were included in the study. The results of the study have been presented as under:

#### **4.1 Prevalence**

Canine kerato-conjunctivitis sicca showed a prevalence rate of 34.92% (22/63) among the ocular affections in dog which were presented during the study period.

#### **4.2 Signalment**

##### **4.2.1 Breed wise distribution of KCS in dogs**

Breed-wise distribution of KCS in dogs revealed that Pugs were affected the highest (70%) followed by Bull dog (10%), Rottweiler (10%) and Non-Descript (10%) (Table 4.1 and Figure 1).

##### **4.2.2 Age – wise distribution of KCS in dogs**

All KCS cases were categorized into age groups of 0-2 yrs, 3-6 yrs, 7-10 yrs and above 10 yrs. The high incidence was recorded in the age group of 7-10 yrs (50%) followed by 3-6 (30%) and 0-2 (20%). No dog was affected in age group of above 10 years (Table 4.2 and Figure 2).

##### **4.2.3 Sex- wise distribution of KCS**

KCS was predominantly observed in male dogs, accounting for 70% of the recorded cases, while females accounted for 30% of the cases in the present study (Table 4.3 and Figure 3).

**Table 4.1 Breed -wise distribution of KCS in dogs (%)**

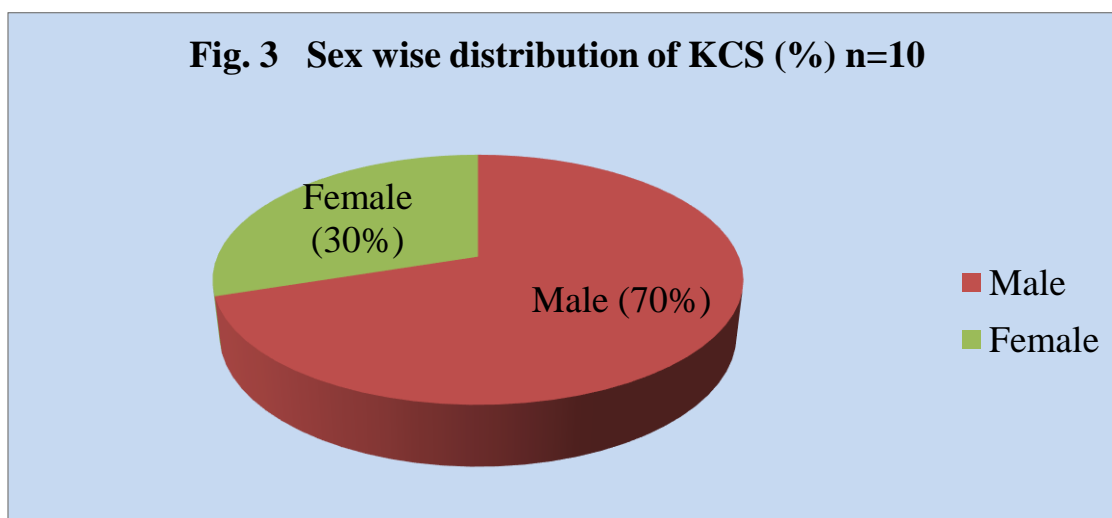
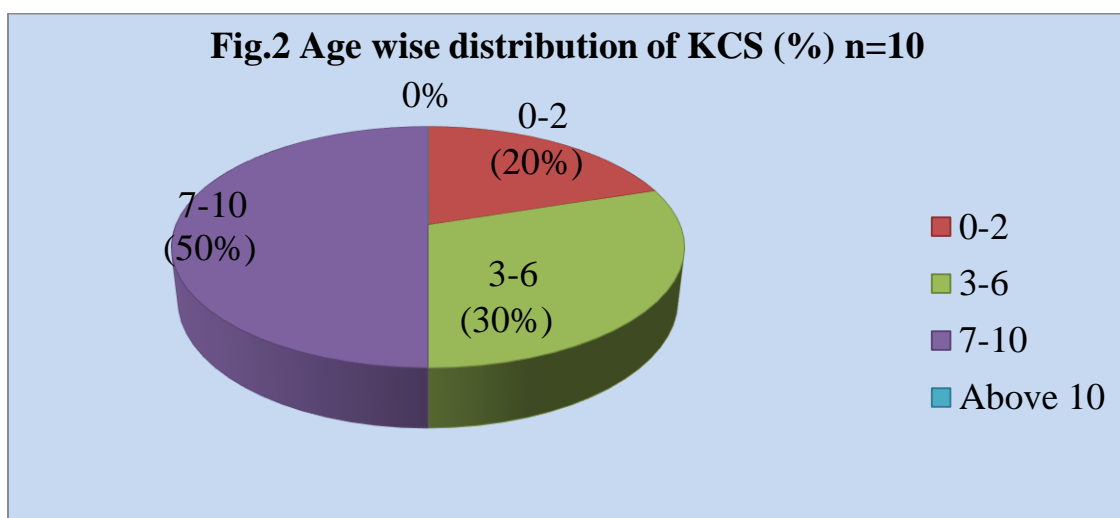
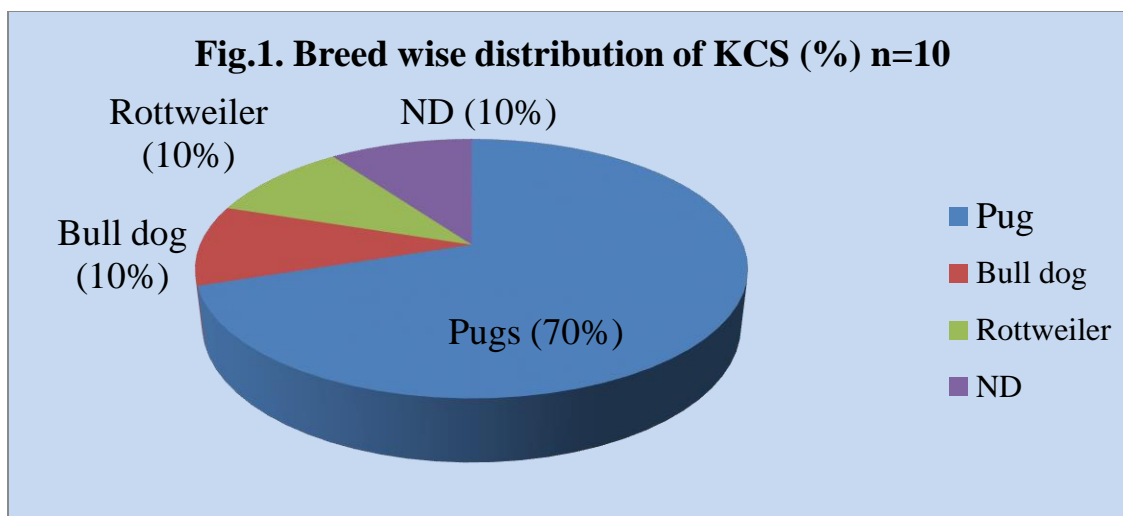
<b>Breed</b>				
<b>No of dogs</b>	<b>Pugs</b>	<b>Rottweiler</b>	<b>Bull dog</b>	<b>ND</b>
n= 10	70% (n=7)	10 (%) (n=1)	10 (%) (n=1)	10 (%) (n=1)

**Table 4.2 Age -wise distribution of KCS in dogs (%)**

<b>Age (in years)</b>				
<b>No of dogs</b>	<b>0-2</b>	<b>3-6</b>	<b>7-10</b>	<b>Above 10</b>
n=10	20% (n=2)	30% (n=3)	50% (n=5)	0% (n=0)

**Table 4.3 Sex -wise distribution of KCS in dogs (%)**

<b>Sex</b>		
<b>No of dogs</b>	<b>Male</b>	<b>Female</b>
n = 10	70% (n = 7)	30% (n = 3)



### **4.3. Case History**

#### **4.3.1 Cause of damage**

Most of the cases presented with KCS had a history of unknown cause (40%), followed by trauma by hitting by a stick (20%), sharp object penetration (10%) and corneal opacity (10%) (Table 4.4, Figure 4).

#### **4.3.2 Ocular discharge**

Ocular discharge was muco-purulent (50%) in most of the affected cases, where as mucoid (30%) and serous discharge (20%) were also noticed (Table 4.5, Figure 5).

#### **4.3.3 Vision**

Vision was absent in five (50%) cases where as it was present in 30% of the dogs and vision was seen partial in 20% of cases (Table 4.6, Figure 6).

#### **4.3.4 Duration of damage (in days)**

Mean  $\pm$ SE of duration of damage (n = 10) of group I and II was  $16.4 \pm 5.60$  and  $16.0 \pm 3.78$  (Table 4.7) and the values were statistically insignificant.

#### **4.3.5 Previous ocular disease**

Previous ocular disease was seen in 80% of cases. Desmatocele was observed in 10% of dogs and maggot infestation were also seen in 10% of dogs.

#### **4.3.6 Prior treatment before presentation**

50% of the affected dogs had not received any previous treatment prior to presentation. However, topical ocular antibiotics had been administered in 40% of dogs and parental antibiotics had been given in 10% (Table 4.8, Figure 7).

#### **4.3.7 Vaccination status**

Vaccination was complete and incomplete in 40% of the affected dogs and not started in 20% of the dogs (Table 4.9 Figure 8).

**Table 4.4 Cause of damage in dogs presented with KCS (%)**

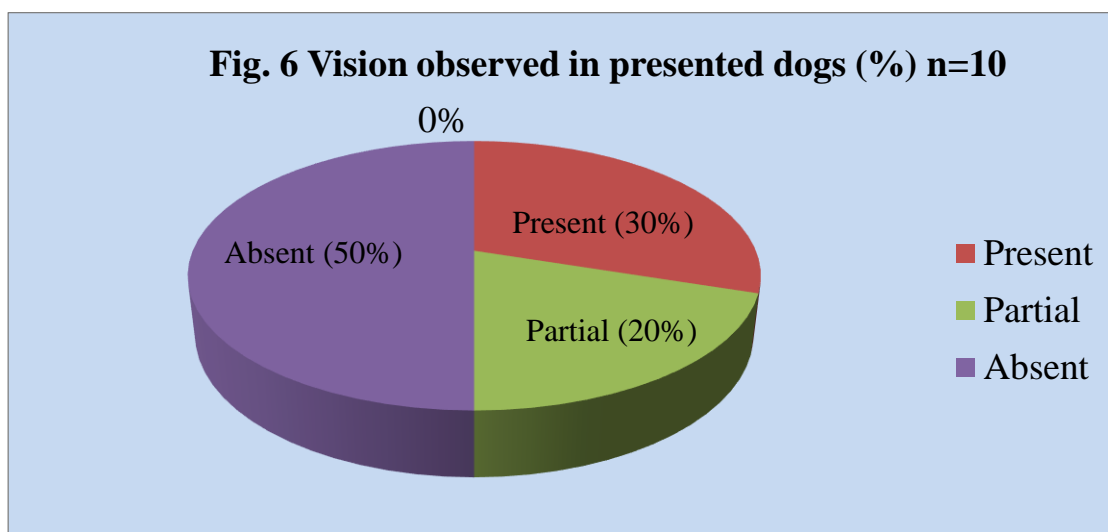
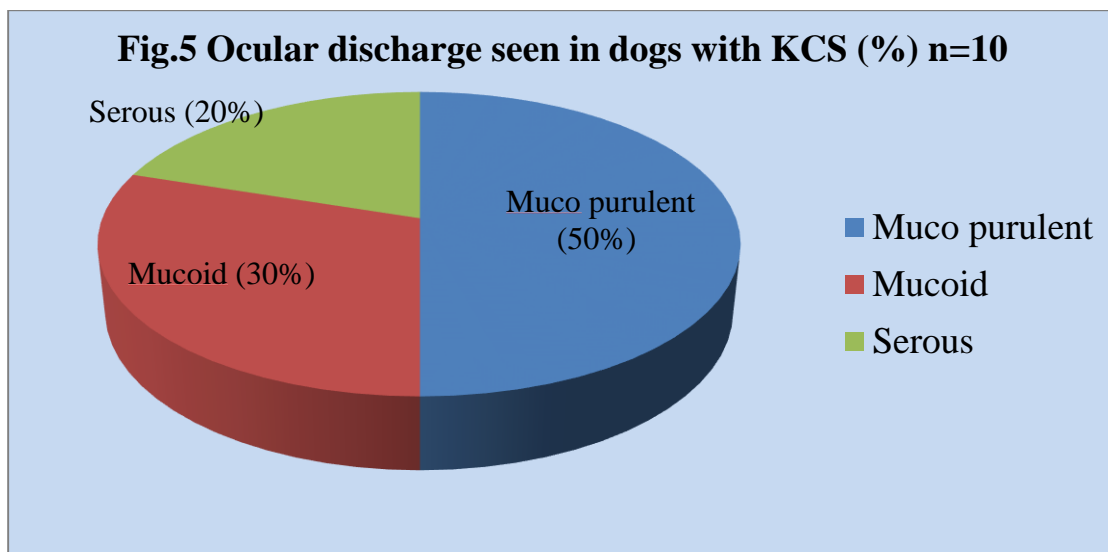
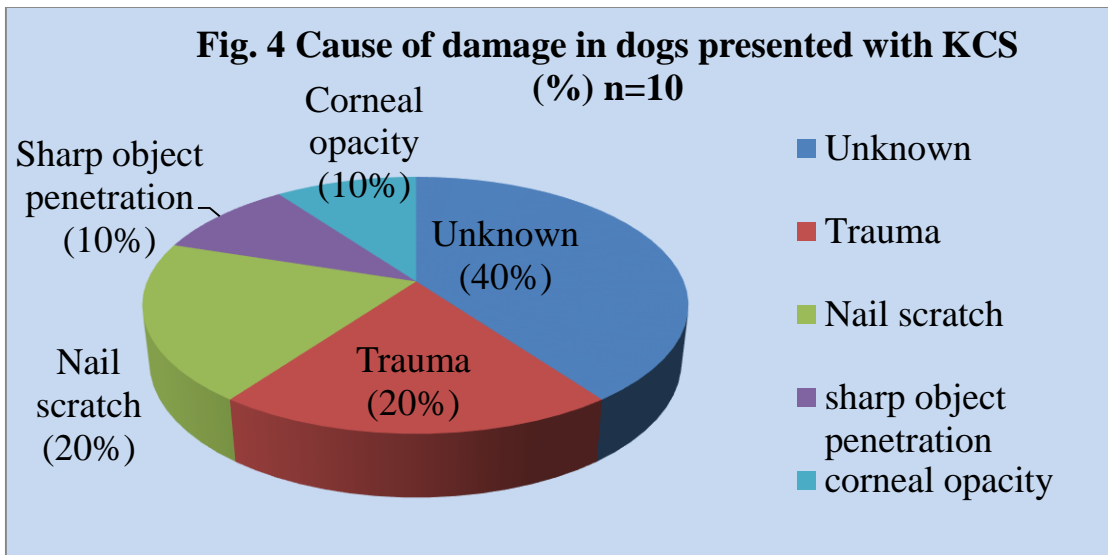
<b>Cause of damage</b> <b>No. of dogs</b>	<b>Unknown</b>	<b>Trauma</b>	<b>Nail scratch</b>	<b>Sharp object penetration</b>	<b>Corneal opacity</b>
n = 10	40% (n =4)	20% (n=2)	20% (n =2)	10% (n=1)	10% (n=1)

**Table 4.5 Ocular discharge seen in dogs with KCS (%)**

<b>Ocular discharge</b> <b>No. of dogs</b>	<b>Serous</b>	<b>Mucoid</b>	<b>Muco-Purulent</b>
n =10	20% n =2	30% n =3	50% n =5

**Table 4.6 Vision observed in presented dogs (%)**

<b>Vision</b> <b>No. of dogs</b>	<b>Present</b>	<b>Absent</b>	<b>Partial</b>
n = 10	30% (n =3)	50% (n =5)	20% (n =2)



**Table 4.7 Duration of damage in KCS affected dogs (%)**

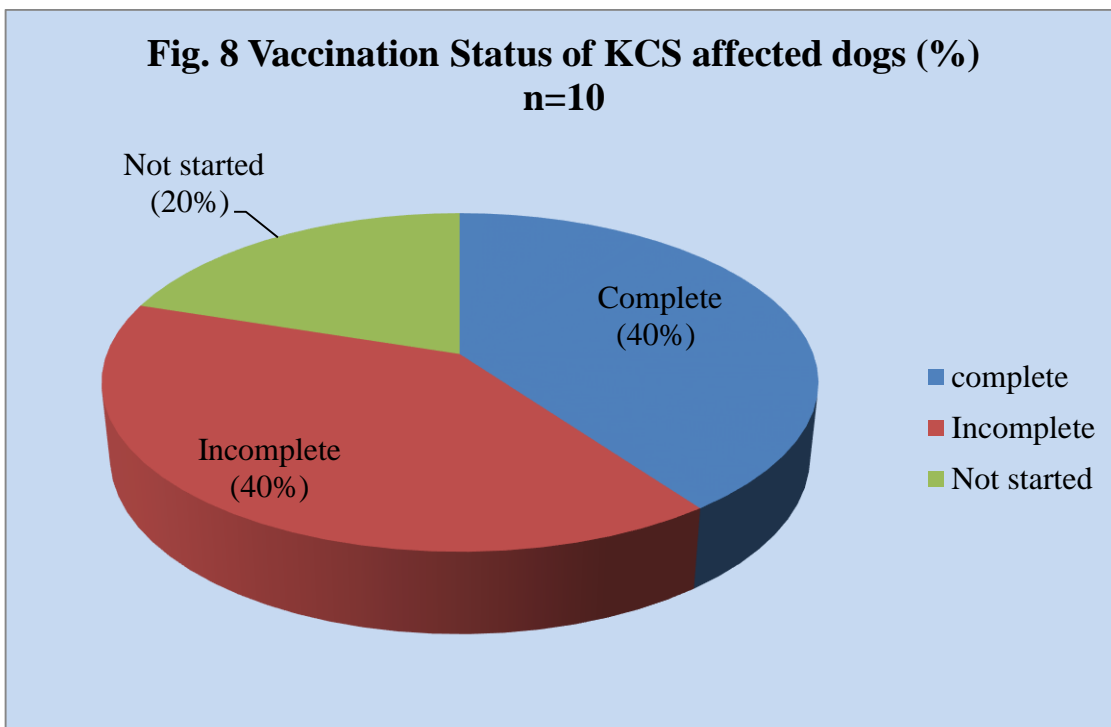
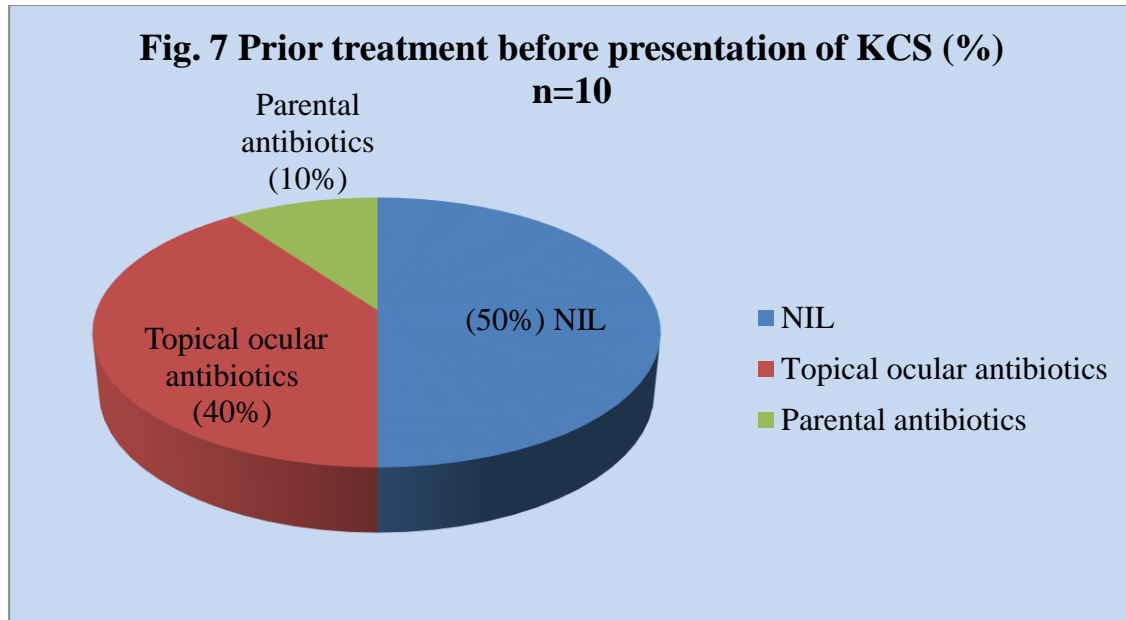
<b>Duration of damage</b> <b>Groups</b>	<b>I</b>	<b>II</b>
Mean $\pm$ SE	16.4 $\pm$ 5.60	16.0 $\pm$ 3.78

**Table 4.8 Prior treatment before presentation of KCS affected dogs (%)**

<b>Prior treatment</b> <b>No. of dogs</b>	<b>Topical ocular antibiotics</b>	<b>Parental antibiotics</b>	<b>No treatment</b>
n = 10	40% (n = 4)	1% (n = 1)	50% (n = 5)

**Table 4.9 Vaccination status of the KCS affected dogs (%)**

<b>Vaccination</b> <b>No. of dogs</b>	<b>Complete</b>	<b>Incomplete</b>	<b>Not started</b>
n = 10	40% (n=4)	40% (n=4)	20% (n=2)



#### 4.4 Physiological parameters

The physiological parameters [rectal temperature (°F), heart rate (beats/min), respiration rate (breaths/min)] recorded pre-treatment and at regular intervals following treatment of the dogs affected with KCS are presented in Table 4.10. All the pre-treatment and post-treatment day parameters were within the normal physiological limits. Non-significant variation was observed in physiological parameters throughout the study period.

**Table 4.10 Physiological parameters on day 0 before treatment and on 15, 30, 45 day post treatment (Mean  $\pm$  SE)**

<b>Groups \ Day</b>	<b>0</b>	<b>15</b>	<b>30</b>	<b>45</b>
<b>Rectal temperature (°F) (Mean <math>\pm</math> SE)</b>				
I	101.3 $\pm$ 0.44	100.9 $\pm$ 0.32	101.8 $\pm$ 0.35	101.8 $\pm$ 0.30
II	101.7 $\pm$ 0.48	101.9 $\pm$ 0.04	101.7 $\pm$ 0.32	101.7 $\pm$ 0.09
<b>Heart rate (beats/min) (Mean <math>\pm</math> SE)</b>				
I	106.6 $\pm$ 7.01	88.6 $\pm$ 5.51	80.4 $\pm$ 5.38	76.8 $\pm$ 2.72
II	101.0 $\pm$ 7.37	86.7 $\pm$ 4.34	90.5 $\pm$ 5.42	89.5 $\pm$ 6.70
<b>Respiration rate (breaths/min) (Mean <math>\pm</math> SE)</b>				
I	31.8 $\pm$ 5.17	23.2 $\pm$ 3.44	26.4 $\pm$ 2.83	23.0 $\pm$ 3.45
II	31.8 $\pm$ 5.40	24.6 $\pm$ 3.65	29.0 $\pm$ 3.40	24.0 $\pm$ 2.36

## **4.5 Ophthalmic examination**

### **4.5.1 Eye affected**

Left eye (60%) was affected more with KCS than the right eye (40%). The results are presented in Table 4.11, Figure 9.

### **4.5.2 Gross examination**

#### **4.5.2.1 Mucous membrane colour**

On gross examination the mucous membrane was congested in 70% cases, pink in 20% and pale in 10% of dogs.(Table 4.12, Figure 10).

#### **4.5.2.2 Photophobia**

Dogs of both the groups, registered a decrease in photophobia as compared to the pre-treatment day 0 values. A steady decline in the grades of photophobia throughout the study period was observed. The pre-treatment value was statistically significant in comparison to the day 45 values (Table 4.13, Figure 11).

#### **4.5.3.3 Rapidity of progression**

There was progressive increase in 50% of the cases. Acute onset was seen in 40% cases, and recurrence was seen in 10% of the cases (Table 4.14, Figure 12).

**Table 4.11 Eyes affected (%)**

<b>Eyes affected</b> <b>No. of dogs</b>	<b>Left</b>	<b>Right</b>
n = 10	60% (n = 6)	40% (n = 4)

**Table 4.12 Mucous membrane colour (%)**

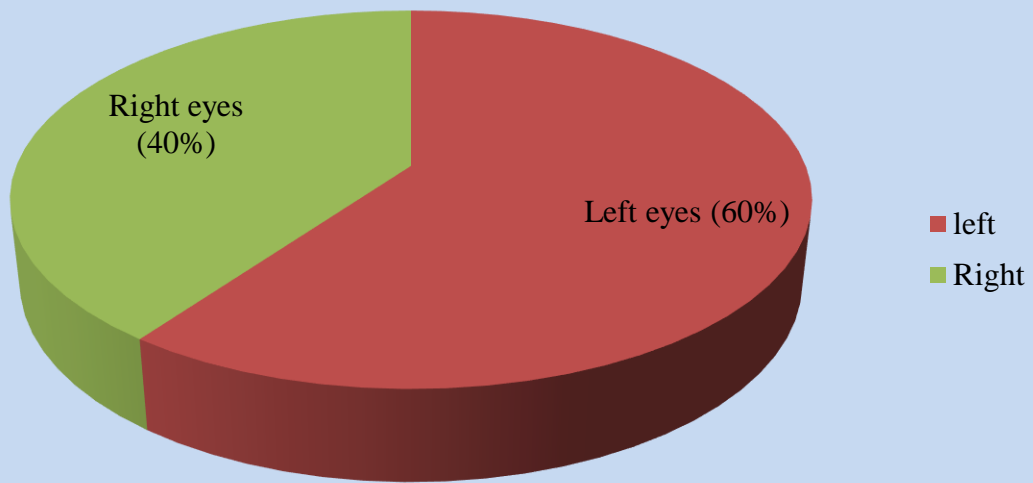
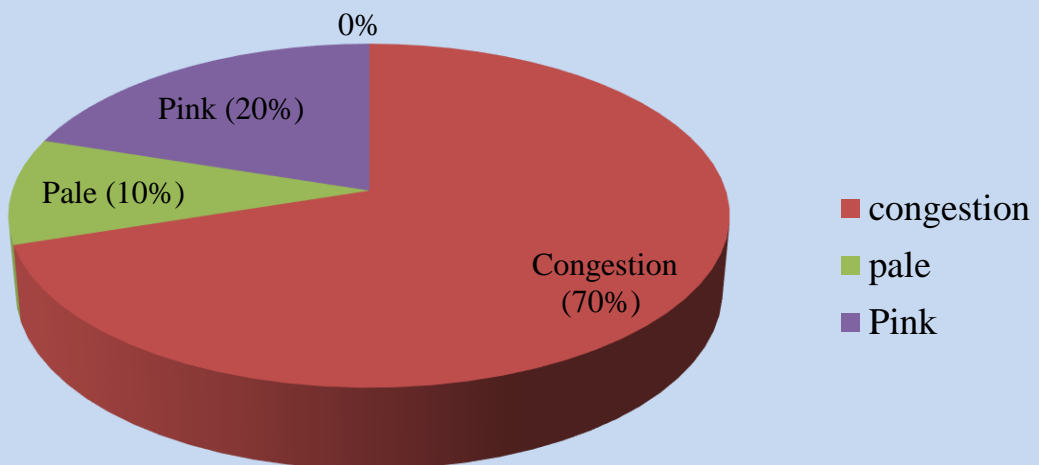
<b>Mucous membrane colour</b> <b>No. of dogs</b>	<b>Congestion</b>	<b>Pale</b>	<b>Pink</b>
n = 10	70% (n = 7)	10% (n = 7)	20% (n = 2)

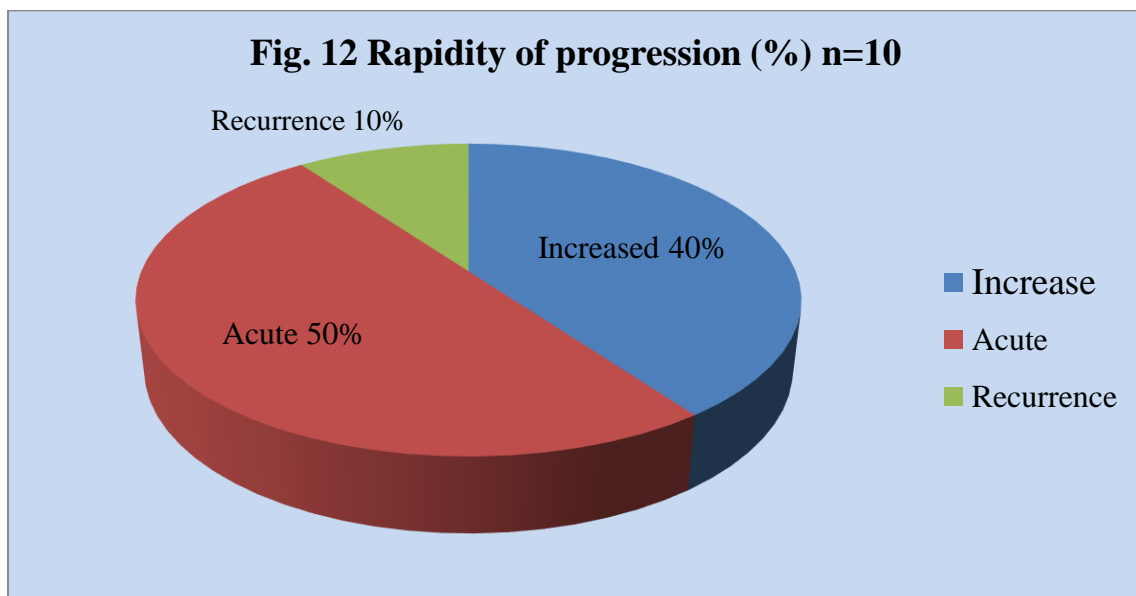
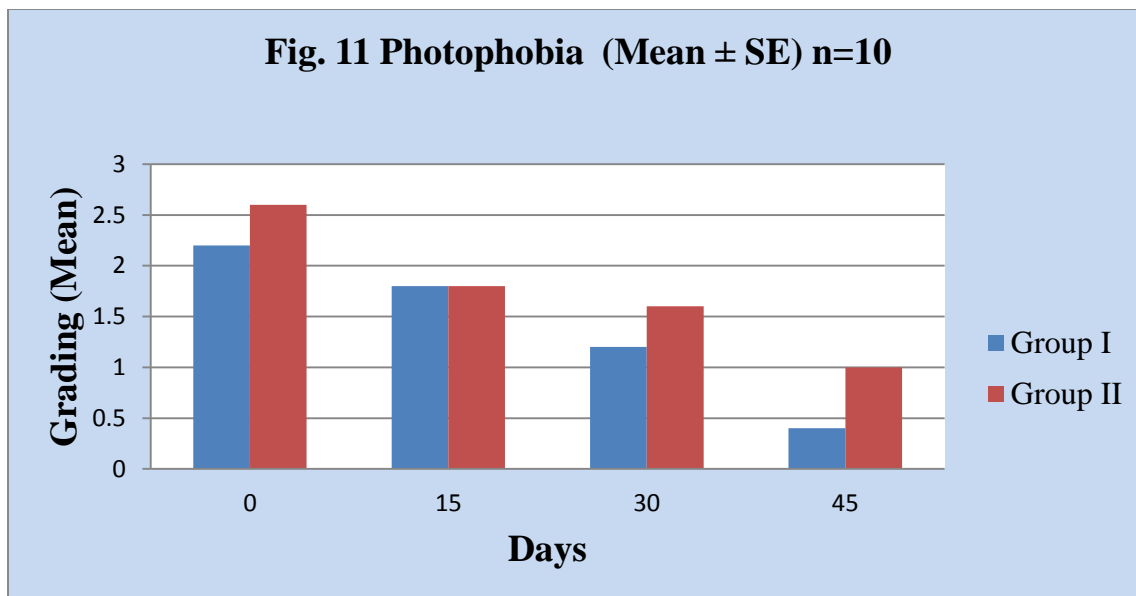
**Table 4.13 Photophobia (%)**

<b>Photophobia</b> <b>Groups</b>	<b>0</b>	<b>15</b>	<b>30</b>	<b>45</b>
I	2.20 ± 0.20 <sup>b</sup>	1.80 ± 0.20 <sup>b</sup>	1.20 ± 0.20 <sup>ab</sup>	0.40 ± 0.24 <sup>a</sup>
II	2.60 ± 0.24 <sup>b</sup>	1.80 ± 0.37 <sup>ab</sup>	1.60 ± 0.24 <sup>a</sup>	1.00 ± 0.31 <sup>a</sup>

**Table 4.14 Rapidity of progression (%)**

<b>Rapidity of progression</b> <b>No. of dogs</b>	<b>Increased</b>	<b>Acute</b>	<b>Recurrence</b>
n = 10	50% (n=5)	40% (n =4)	10% (n =1)

**Fig. 9 Eyes affected (%) n=10****Fig. 10 Mucous membrane colour (%) n=10**



#### 4.5.4 Neuro-ophthalmic examination

Pre-treatment and postoperative assessment of all the neuro-ophthalmic tests (Pupillary light reflex (PLR), Cotton ball test, Dazzle reflex test, Palpebral reflex, Menace reflex test, Visual placing postural reaction) performed in all the cases during the study period showed improvement on post-treatment days 15, 30 and 45 day as compare to day 0 described by Slatter (2001). Neuro-ophthalmic test results are represented in Table 4.15.

**Table 4.15: Neuro-ophthalmic tests on day 0 before treatment and on 15, 30, 45 day post-treatment**

Pupillary Light Reflex												
Day Gr	0			15			30			45		
	+	+/-	-	+	+/-	-	+	+/-	-	+	+/-	-
I	-	2 (40%)	3 (60%)	1 (20%)	4 (80%)	-	3 (60%)	2 (40%)	-	5 (100%)	-	-
II	-	2 (40%)	3 (60%)	1 (20%)	4 (80%)	-	4 (80%)	1 (20%)	-	5 (100%)	-	-
Cotton Ball test												
Day Gr	0			15			30			45		
	+	+/-	-	+	+/-	-	+	+/-	-	+	+/-	-
I	-	2 (40%)	3 (60%)	1 (20%)	4 (80%)	-	3 (60%)	2 (40%)	-	5 (100%)	-	-
II	-	1 (20%)	4 (80%)	-	2 (40%)	3 (60%)	-	2 (40%)	3 (60%)	-	4 (80%)	1 (20%)
Dazzle Test												
Day Gr	0			15			30			45		
	+	+/-	-	+	+/-	-	+	+/-	-	+	+/-	-
I	-	2 (40%)	3 (60%)	1 (20%)	3 (60%)	1 (20%)	2 (40%)	3 (60%)	-	5 (100%)	-	-
II	-	1 (20%)	4 (80%)	1 (20%)	4 (80%)	-	3 (60%)	2 (40%)	-	5 (100%)	-	-
Palpebral Reflex												
Day Gr	0			15			30			45		
	+	+/-	-	+	+/-	-	+	+/-	-	+	+/-	-
I	5 (100%)	-	-	-	-	-	-	-	-	-	-	-
II	5 (100%)	-	-	-	-	-	-	-	-	-	-	-
Menace Reflex												
Day Gr	0			15			30			45		
	+	+/-	-	+	+/-	-	+	+/-	-	+	+/-	-
I	-	2 (40%)	3 (60%)	1 (20%)	4 (80%)	-	3 (60%)	2 (40%)	-	5 (100%)	-	-
II	-	2 (40%)	3 (60%)	1 (20%)	4 (80%)	-	4 (80%)	1 (20%)	-	5 (100%)	-	-
Visual Postural Reflex												
Day Gr	0			15			30			45		
	+	+/-	-	+	+/-	-	+	+/-	-	+	+/-	-
I	-	2 (40%)	3 (60%)	1 (20%)	4 (80%)	-	2 (40%)	3 (60%)	-	4 (80%)	1 (20%)	-
II	-	1 (20%)	4 (80%)	1 (20%)	3 (60%)	1 (20%)	1 (20%)	4 (80%)	-	1 (20%)	4 (80%)	-

## **4.6 Diagnostic tests**

### **4.6.1 Schirmer tear test- I**

In group I, a mean  $\pm$  SE values for Schirmer tear test (STT-I) was observed to be  $3.20 \pm 1.32$  mm/min and for group II dogs was  $5.80 \pm 0.37$  mm/min. Both groups showed an increasing STT- I values in comparison to pre-treatment values, after commencement of treatment. Statistical significant increase was observed in all the dogs of group I and II as compare to pre-treatment day 0. The results are presented in Table 4.16, Figure 13.

### **4.6.2 Schirmer tear test-II**

Decreased readings of Schirmer tear test (STT-II) was significant in group I and II in the Keratoconjunctivitis sicca affected dogs. The values were in increasing trend from pre-treatment values through out the observation period. The details are presented in the Table 4.17, Figure 14.

### **4.6.3 Tear film Break-Up Time**

Decreased tear film breakup time (TFBUT) in dogs of group I and II affected with Keratoconjunctivitis sicca was seen on day 0. Both groups showed an increasing TFBUT values from 30 day to 45 day in comparison to pre-treatment values as represented in the Table 4.18, Figure 15.

**Table 4.16 Schirmer tear test-I (STT-I)**

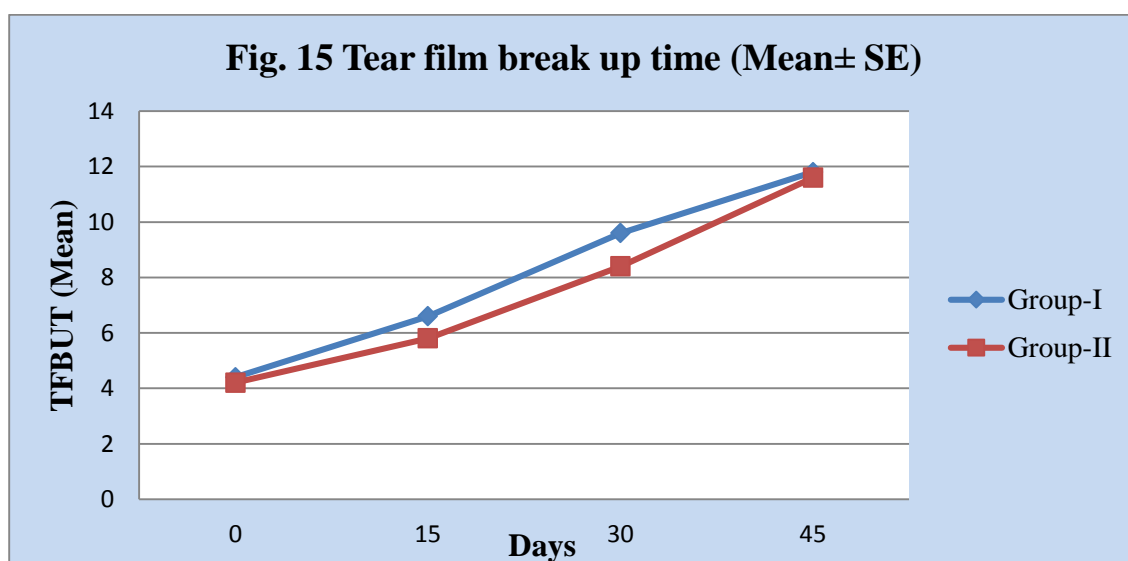
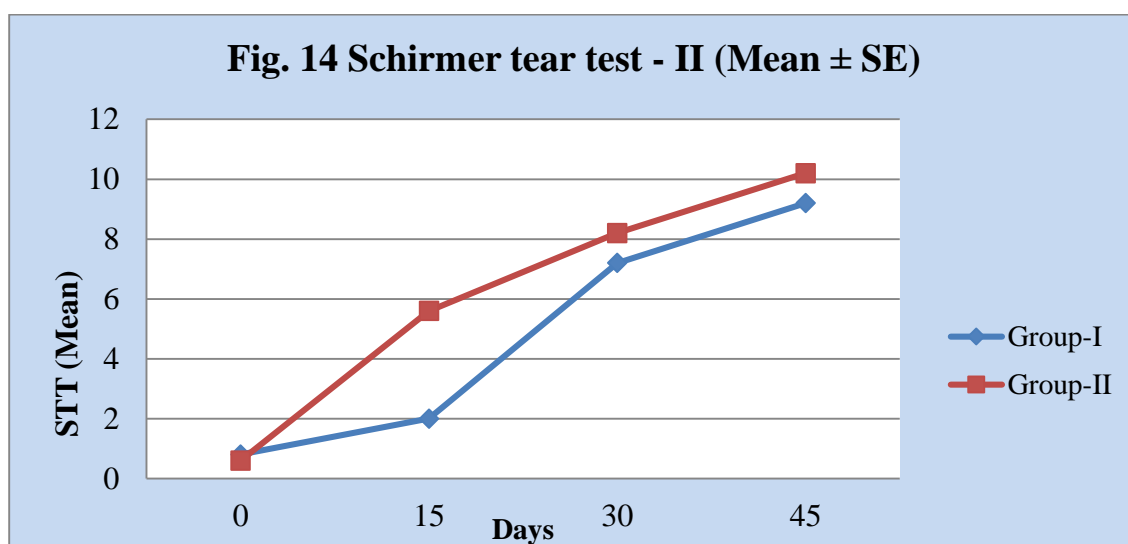
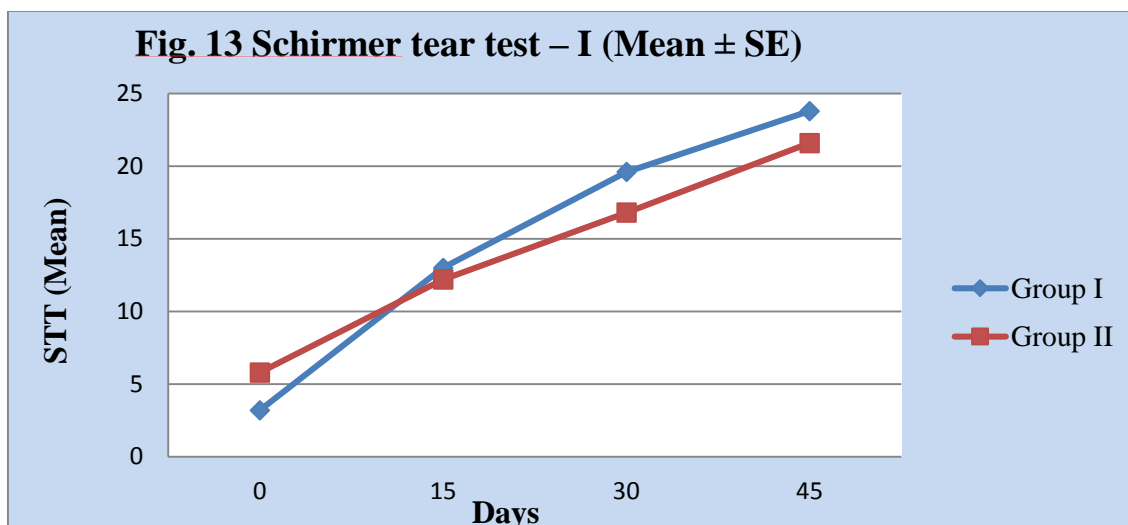
<b>Group \ Day</b>	0	15	30	45
<b>I</b>	3.20 ± 1.32 <sup>a</sup>	13.00 ± 2.28 <sup>b</sup>	19.6 ± 2.90 <sup>bc</sup>	23.80 ± 2.76 <sup>c</sup>
<b>II</b>	5.80 ± 0.37 <sup>a</sup>	12.2 ± 0.80 <sup>b</sup>	16.8 ± 1.35 <sup>b</sup>	21.6 ± 2.73 <sup>c</sup>

**Table 4.17 Schirmer tear test-II (STT-II)**

<b>Group \ Day</b>	0	15	30	45
<b>I</b>	0.80 ± 0.200 <sup>a</sup>	2.00 ± 0.00 <sup>b</sup>	7.20 ± 0.37 <sup>c</sup>	9.20 ± 0.20 <sup>d</sup>
<b>II</b>	0.60 ± 0.24 <sup>a</sup>	5.60 ± 0.51 <sup>b</sup>	8.20 ± 0.20 <sup>c</sup>	10.20 ± 0.37 <sup>d</sup>

**Table 4.18 Tear film break-up time (TFBUT)**

<b>Group \ Day</b>	0	15	30	45
<b>I</b>	4.40 ± 0.92 <sup>a</sup>	6.60 ± 1.24 <sup>ab</sup>	9.6 ± 1.91 <sup>bc</sup>	11.8 ± 1.82 <sup>c</sup>
<b>II</b>	4.20 ± 0.58 <sup>a</sup>	5.8 ± 0.97 <sup>a</sup>	8.4 ± 1.03 <sup>b</sup>	11.6 ± 0.67 <sup>c</sup>



## **4.7 Microbiological examination**

### **4.7.1 Antibiotic sensitivity test (ABST)**

The seven antibiotics were used in the present study for ABST. Gentamicin showed maximum sensitivity of 100% and Moxifloxacin showed intermediate sensitivity of 70% and was sensitive to the extent of 10%. Interpretation of antibiotic pattern of the antibiotics is presented in Table 4.19.

## **4.8 Biochemical analysis**

Blood glucose, total protein, serum albumin, serum globulin were estimated in all the affected cases on day 0, 15, 30 and 45 days post-treatment. Non-significant statistical variation was observed in the values in both the groups were within normal physiological range. Analysis of biochemical parameters is presented in Tables 4.20, 4.21, 4.22, 4.23.

## **4.9 Haematological estimations**

Haematological parameters estimated on day 0 are presented in Table 4.24. The values were within the normal range and were statistically non-significant.

**Table 4.19 Antibiogram pattern interpretation performed pre-treatment on day 0**

Groups (n=5)	Bacitracin <sup>10</sup> (%)			Polymyxin B <sup>300</sup> (%)			Tobramycin <sup>30</sup> (%)			Gentamicin <sup>30</sup> (%)		
	S	I	R	S	I	R	S	I	R	S	I	R
I	60.00 (n=3)	20.00 (n=1)	20.00 (n=1)	80.00 (n=4)	-	20.00 (n=1)	80.00 (n=4)	-	20.00 (n=1)	100 (n=5)	-	-
II	40.00 (n=2)	-	60.00 (n=3)	80.00 (n=4)	-	20.00 (n=1)	20.00 (n=1)	60.00 (n=3)	20.00 (n=1)	100 (n=5)	-	-
Total (n=10)	50.00 (n=5)	10.00 (n=1)	40.00 (n=4)	80.00 (n=8)	-	20.00 (n=2)	50.00 (n=5)	30.00 (n=3)	20.00 (n=2)	100 (n=10)		

Groups (n=5)	Moxifloxacin <sup>5</sup> (%)			Neomycin <sup>30</sup> (%)			Ciprofloxacin <sup>10</sup> (%)			Gatifloxacin <sup>30</sup> (%)		
	S	I	R	S	I	R	S	I	R	S	I	R
I	-	80.00 (n=4)	20.00 (n=1)	-	-	100 (n=5)	20.00 (n=1)	60.00 (n=3)	20.00 (n=1)	60.00 (n=3)	20.00 (n=1)	20.00 (n=1)
II	20.00 (n=1)	60.00 (n=3)	20.00 (n=1)	-	-	100 (n=5)	20.00 (n=1)	20.00 (n=1)	60.00 (n=3)	60.00 (n=3)	-	40.00 (n=2)
Total (n=10)	10.00 (n=1)	70.00 (n=7)	20.00 (n=2)	-	-	100 (n=10)	20.00 (n=2)	40.00 (n=4)	40.00 (n=4)	60.00 (n=6)	10.00 (n=1)	30 (n=3)

**Table 4.20 Biochemical estimation (Mean  $\pm$  SE)**

<b>Day</b> <b>Group</b>	<b>0</b>	<b>15</b>	<b>30</b>	<b>45</b>
<b>I</b>	107.2 $\pm$ 21.8	106.2 $\pm$ 21.9	105.4 $\pm$ 15.8	105.8 $\pm$ 12.08
<b>II</b>	105.2 $\pm$ 14.8	104.8 $\pm$ 12.8	104.2 $\pm$ 12.9	103.7 $\pm$ 11.4
<b>Total protein estimation (mg/dl) (Mean <math>\pm</math> SE)</b>				
<b>I</b>	7.68 $\pm$ 0.59	5.77 $\pm$ 0.47	7.27 $\pm$ 1.32	7.02 $\pm$ 1.62
<b>II</b>	7.78 $\pm$ 0.61	7.58 $\pm$ 0.48	7.37 $\pm$ 1.43	7.17 $\pm$ 1.73
<b>Serum Albumin estimation (mg/dl) (Mean <math>\pm</math> SE)</b>				
<b>I</b>	3.1 $\pm$ 0.44	2.87 $\pm$ 0.55	2.39 $\pm$ 0.31	3.16 $\pm$ 0.78
<b>II</b>	4.1 $\pm$ 0.88	3.2 $\pm$ 0.55	2.9 $\pm$ 0.66	2.2 $\pm$ 0.32
<b>Serum Globulin estimation (g/dl) (Mean <math>\pm</math> SE)</b>				
<b>I</b>	4.63 $\pm$ 0.87	3.01 $\pm$ 0.23	4.96 $\pm$ 1.05	3.59 $\pm$ 1.05
<b>II</b>	4.97 $\pm$ 1.06	4.64 $\pm$ 0.88	3.5 $\pm$ 0.32	3.60 $\pm$ 1.05

**Table 4.24 Haematological estimation (day 0)**

				<b>DLC</b>				
<b>Group</b>	<b>Hb (g/dl)</b>	<b>TLC (Nx10<sup>3</sup>/<math>\mu</math>l)</b>	<b>PCV (%)</b>	<b>N (%)</b>	<b>L (%)</b>	<b>M (%)</b>	<b>E (%)</b>	<b>B (%)</b>
<b>I</b>	11.38 $\pm$ 0.41	10.19 $\pm$ 0.63	32.8 $\pm$ 0.73	68.20 $\pm$ 1.28	20.26 $\pm$ 1.28	4.94 $\pm$ 1.16	3.60 $\pm$ 1.16	0.00 $\pm$ 0.00
<b>II</b>	11.44 $\pm$ 0.91	11.16 $\pm$ 0.22	35.6 $\pm$ 1.80	62.80 $\pm$ 1.48	28.20 $\pm$ 1.12	4.60 $\pm$ 0.87	4.40 $\pm$ 0.67	0.00 $\pm$ 0.00

## **4.10 Management of KCS**

### **4.10.1 Medical Therapy**

The therapeutic efficacy of the cyclosporine against keratoconjunctivitis sicca (KCS) in group I was judged based on the improvement in clinico-ophthalmic signs and ocular surface tests values returning to normal levels. Dogs belonging to Group I were administered with topical application of cyclosporine ophthalmic ointment\* (2mg/gm) b.i.d, q 12 hr throughout the treatment period, methylcellulose eye drops q.i.d, q 4 hr and Gatifloxacin/ Moxifloxacin drops t.i.d for 2 weeks. The dogs in the group showed improvement in clinico- ophthalmic signs within 6 weeks of treatment. The increase in STT-I and II, TFBUT were found significant after 45 days of treatment. The regimen showed good therapeutic efficacy in all (100%) dogs.

### **4.10.2 Surgical management**

Five dogs affected with KCS of either sex were included in the clinical study. The ophthalmic examination was easily performed in all the dogs without any chemical restraint.

#### **4.10.2.1 Anaesthesia**

All surgical manipulations were done under atropine @0.04 mg/kg b.wt, xylazine hydrochloride @2 mg/kg b.wt, ketamine hydrochloride @10 mg/kg b.wt and diazepam combinations and these were adequate to provide analgesia.

#### **4.10.2.2 Surgical technique**

Parotid duct transposition technique (PDT) was performed in all the five cases of group II. Restrain of dogs in lateral recumbency with the affected side upwards, provided adequate exposure to the eye and surrounding structures. Cannulation of parotid duct with 24G catheter helped for easy identification. The surgery involved re- routing the parotid salivary duct from its destination at the parotid papilla in the mouth to the ventral conjunctival sac and papilla was sutured in place by using 6/0 polygalactin suture and the cases were monitored up to 45<sup>th</sup> day of surgery.

### 4.10.3 Post- operative treatment

Flurbiprofen drops t.i.d., Gatifloxacin/ Moxifloxacin drops q.i.d., were instilled topically for two weeks post-operatively in group – II which reduced the corneal edema and irritation. The changes in demeanour, pawing/ rubbing were not recorded in any dog. Methylcellulose eye drops t.i.d, for two weeks helped in providing immediate lubrication to the affected eyes in both the groups. Elizabeth collar was effective to prevent self-mutilation. The owners were advised to give meals in small quantities frequently in order to provide a regular wetting on the surface of eye in group-II.

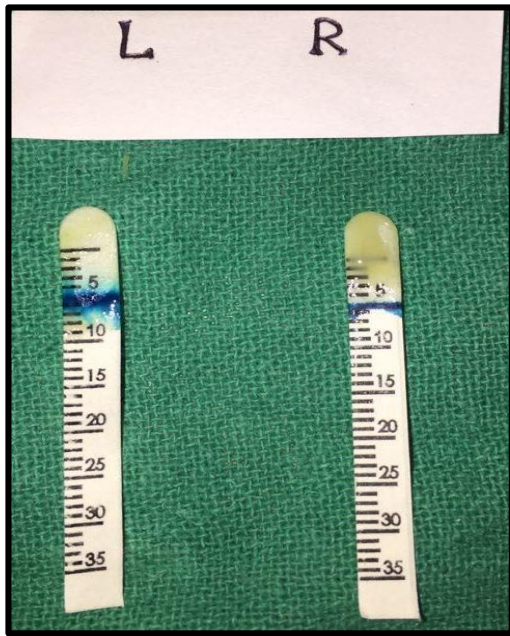
### 4.11 Post-operative outcome, complications and their management

Re-evaluation at every fifteen days interval upto 45 day in all cases showed improvement in ocular health as confirmed by increase in the STT I, II and TFBUT values in both the groups. Group-I dogs showed better results of STT-I (643.75%) as compared to dogs of group-II but the test results of STT-II and TFBUT showed better improvement in dogs of group-II as represented in Table 4.25. Improvement in ocular signs post-medication is depicted in Plate no.7 and 8 and post-operative findings of group-II is presented in Plate no.9. Minor complications were observed after parotid duct transposition is shown in Plate no 10.

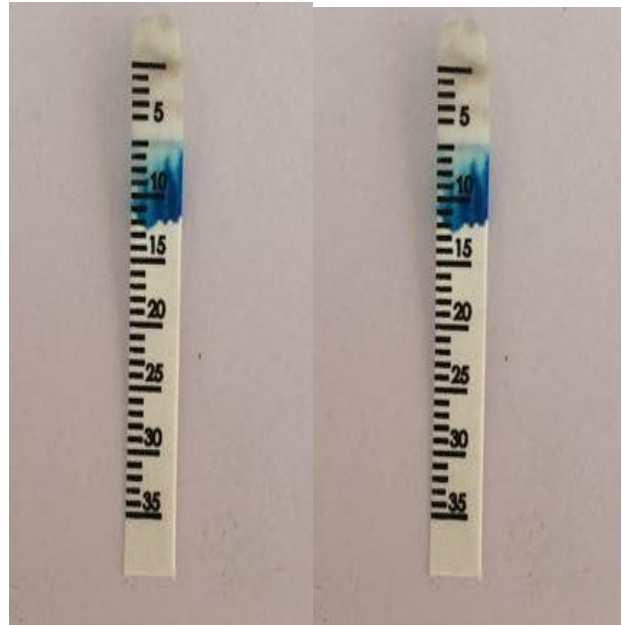
**Table 4.25 Improvement percentage (%)**

<b>Group</b> \ <b>Tests</b>	<b>STT-I</b>	<b>STT-II</b>	<b>TFBUT</b>
I	643.75	1050	168.18
II	272.41	1600	176.19

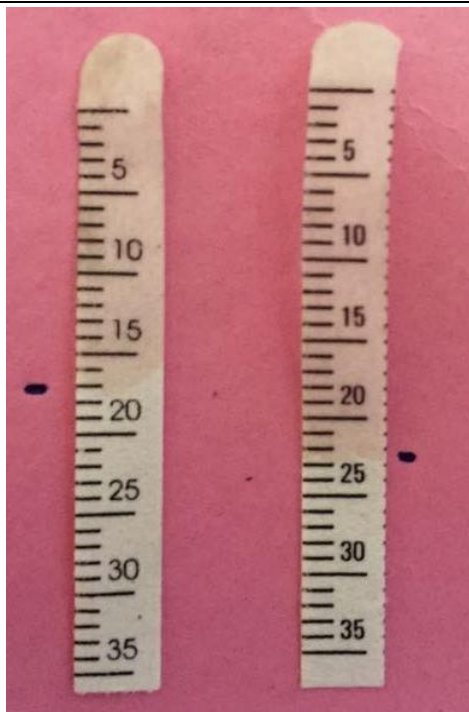
**Plate 7: STT Readings of Medicinal treatment group-I**



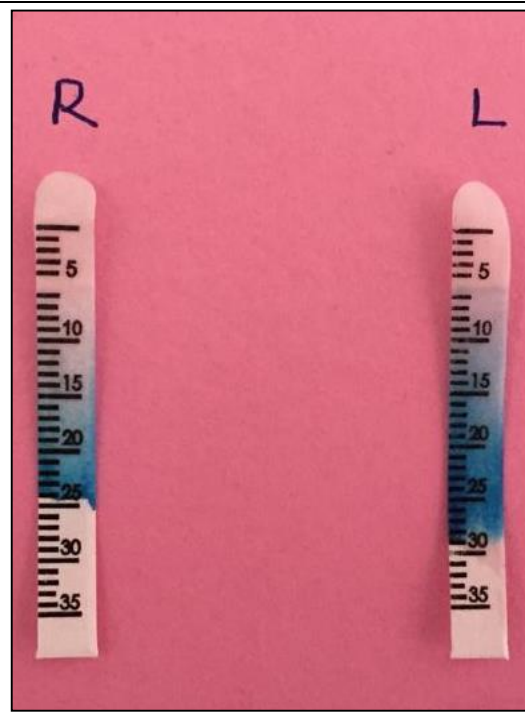
7a: Day 0 (L= 7mm/min, R=6mm/min)



7b: Day 15 (L= 12mm/min, R=12mm/min)





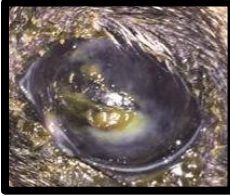









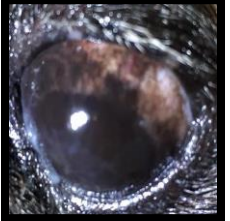







7c: Day 30 (R= 18mm/min, L=22 mm/min)



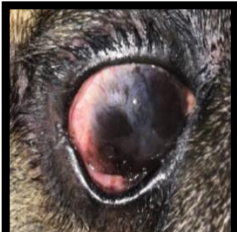
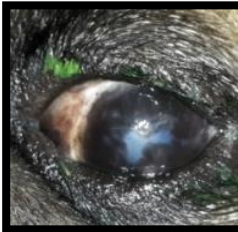

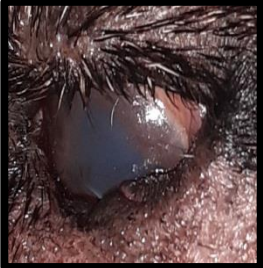
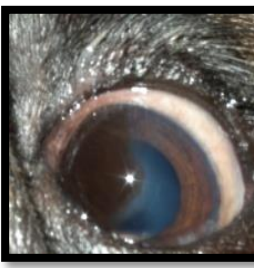
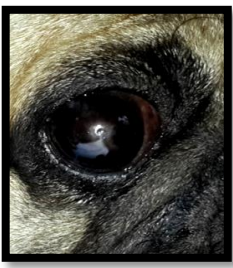




7d: Day 45 (R= 25mm/min, L= 29 mm/min)

**Plate 8: Medicinal Therapy group-I : Improvement shown after cyclosporine application in KCS affected dogs**

Case	1	2	3	4	5
Day					
Day 0					
Day 15					
Day 30					
Day 45					

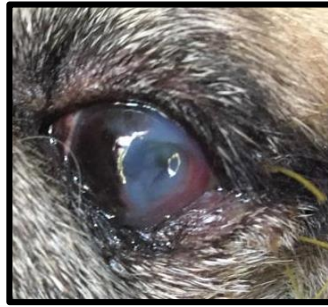
**Plate 9: Post-operative findings in group-II dogs**

Day \ Case	1	2	3	4	5
0					
45					

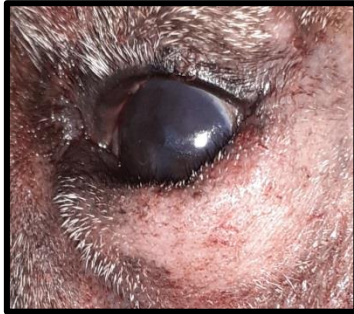
**Plate 10: Post-operative complications observed in group-II**



10a: Over wetting



10b: Corneal ulceration



10c: corneal oedema



10d: Stenosis of parotid duct



**CHAPTER – 5**  
**DISCUSSION**

### DISCUSSION

Dog is considered as an important companion in the modern day life. The diseases of canine eye play an important role in the life of the dog. The emotional upheaval in the owners due to eye related disorders and blindness in companion animals has dictated a positive impact on development of small animal ophthalmology. Important conditions like cataract, glaucoma etc. many a times go unnoticed by the owners which leads to serious disease like kerato-conjunctivitis sicca, corneal ulceration, traumatic conditions, etc. If not attended immediately these conditions may lead to changes in vision and gradually many culminate in blindness or loss of the eye in some cases (Nagaraj, 2011).

The present study was conducted on ten dogs affected with KCS to study the prevalence, efficacy of therapeutic medication and surgical management by parotid duct transposition. The affected dogs were randomly assigned to two treatment groups of five cases each in which topical medication with cyclosporine or surgical management with parotid duct transposition was performed.

#### 5.1 Prevalence

During the study period (August 2018- June 2019) one thousand fourteen hundred eighty eight (1498) dogs were presented to Teaching Veterinary Clinical Complex, out of which seven hundred two (702) were canine cases and sixty three (63) dogs were affected with ocular affections. Twenty two (22) dogs had confirmed kerato-conjunctivitis sicca (KCS) based on Schirmer tear test (STT-I) (<15 mm/min) and (STT II) (<10mm/min) with or without associated ocular affections. The ten dogs affected exclusively with kerato-conjunctivitis sicca were included for the present study.

The prevalence of canine kerato-conjunctivitis sicca (KCS) among ocular affections in dogs was found to be 34.92% (22/63). Kaswan *et al.* (1985) and Ramani *et al.* (2017) recorded a high prevalence of KCS to the extent of 35% and 52.50%, respectively in their various studies. Gelatt *et al.* (2011) reported higher 27.4% prevalence of KCS in diabetic dogs when compared with non- diabetic dogs (15.4%).

However, low prevalence up to 4% (Pierce and Williams, 2006), 7.16% (Nagaraj, 2011) and 14.62% (Krecny *et al.*, 2015) has been recorded in different breeds affected with KCS.

The above variations could be due to, prevalence of infectious/ metabolic diseases and radiation (U-V light) and different environmental/ geographical/ management conditions, temperamental/ behavioral responses, as also recorded by Sapienza *et al.* (2014).

## **5.2 Signalment**

### **5.2.1 Breed wise distribution of KCS in dogs**

The most common breed in the present study were Pug (70%) followed by Bull dog (10%), Rottweiler (10%) and Non-descript (10%). It was observed that, purebred (70%) dogs were found to be more affected than the cross breed and non-descript dogs (30%). The findings of the study collaborates with the observation of Ramani *et al.* (2017) who also observed higher incidence in Chinese Pugs. Dodi (2015) and Krecny *et al.* (2015) have also observed that brachycephalic breeds (English Bull Dog, Lhasa Apsos, Shih Tzu, West Highland White Terriers, Pugs, Pekingeses) are more predisposed to KCS because of genetic predisposition of pure breeds (Gelatt and Brooks, 1999).

During the present study similar finding were observed in Pug breed which might be attributed to relative popularity of this breed locally and subsequently their higher presentation during the study period. Their brachycephalic nature with protrusion of eyeballs, large cornea, exposure keratosis, eyelid abnormalities and xerophthalmia resulting due to shallow and incomplete rim of orbits, congenital abnormalities due to inbreeding, geriatric prevailing diseases. Like cataract, glaucoma, etc. also increases their prevalence to KCS as also observed by Ramani *et al.* (2017).

### **5.2.2 Age wise distribution of KCS in dogs**

KCS cases were recorded more in middle to old aged dogs i.e. 7-10 years (50%), 3-6 years (30%) followed by 0-2 years (20%). This is in agreement with Balicki *et al.*

(2008), Matheis *et al.* (2012) and Ramani *et al.* (2017) who also recorded highest incidence 52.50% in old aged dogs (5 to 15 year age group).

Mean age of KCS has been recorded as 5yrs (Sapienza *et al.*, 2014) and 2.2 and 2.8 yrs (Krecny *et al.*, 2015). Hartley *et al.* (2006) reported that it is difficult to determine the exact age of onset and cases will be referred at varying stages of progression if not years and employing of specialized diagnosis could assist in early detection of eye disorders.

From the present study incidence of KCS was observed highest in middle to old aged dogs and increased with the advancement of age due to poor and unhygienic management practices of owners delayed identification of condition and treatment because of associated infectious causes. Similar observations of compromised immunity, afflictions with Canine Distemper, viral and infectious diseases or vulnerability of eyes to trauma, have been made by Gelatt (2000).

### **5.2.3 Sex wise distribution of KCS in dogs**

The sex- wise distribution revealed that, seven male dogs (70%) were affected with KCS as compared to three female dogs (30%). The incidence rate was similar to as reported by Berdoulay *et al.* (2005), Balicki *et al.* (2008) and Ramani *et al.* (2017) who also reported higher incidence in male dogs (55.00%) than females (45.00%) respectively. The high prevalence could be attributed to the reason that male dogs are preferred more as pets than females dogs due to their outdoor activities and therefore their more presentation. However, Matheis *et al.* (2012) has observed a higher prevalence of KCS in female (72.72%) dogs.

## **5.3 Case History**

### **5.3.1 Cause of damage**

A variety of causes have been suggested as a cause for KCS. In the present study, the cause of KCS was unknown in four cases (60%) and trauma due to various causes like nail scratch (20%), sharp object penetration (10%) and corneal opacity (10%) were also observed. It is seen that the brachycephalic breeds have cornea that is naturally

exposed to environment and makes them more prone to external injuries. Moore (1999) has reported that immune mediated is the most common cause of KCS in dogs whereas, Berger *et al.* (1995), Saito and Kotani (2001), Herrera *et al.* (2007) Matheis *et al.* (2012) and Dodi, (2015) have reported drug induced, iatrogenic, metabolic, congenital, infectious, radiation, neurogenic as the common causes for KCS in dogs. In the present research, the cause of damage was mostly unknown and trauma due to various causes was also observed (Berdoulay *et al.*, 2005). This could be attributed to the protruding eye balls and cornea in brachycephalic as also observed by Ramani *et al.* (2017).

### **5.3.2 Ocular discharge**

In most of the affected cases the eye discharge was muco-purulent (50%) whereas mucoid (30%) and serous discharge (20%) were also noticed. Traumatic irritation to the cornea and conjunctiva stimulates the ocular response there by increasing mucus production by the goblet cells in the conjunctiva which causes a muco-purulent ocular discharge that was seen in both the groups on first day of examination. Berdoulay *et al.* (2005) also reported similar findings in his study where discharge varied from mucoid to muco-purulent and was evident in the conjunctival fornix leading to blepharitis or periocular dermatitis which remains adherent to the cornea.

### **5.3.3 Vision**

During the present investigation, the vision was absent in five cases (50%), where as it was present in three cases (30%) and partially present in two cases (20%). Similar findings have been reported by Moore (1990) who observed that the important causes of reduced vision in KCS were attributed to the conditions of cornea viz. changes in corneal stromal architecture contributing to blood vessel migration, corneal pigmentation, corneal edema, opacity, which disrupts the corneas transparency resulting in reduced or no vision. Decrease in vision was also due to compromise of either of the active pumping mechanism of corneal endothelium or barrier in function of anterior corneal epithelium which causes corneal stroma to develop edema or ulceration. Nagaraj (2011) also reported loss of visual acuity in 30% of the affected cases of KCS. The early diagnosis is

of vital importance to prevent blindness in dogs because KCS is slow, progressive and insidious in nature as also reported by Berdoulay *et al.* (2005).

#### **5.3.4 Duration of damage**

Average duration of damage (in days) was observed to be  $16.4 \pm 5.60$  and  $16.0 \pm 3.78$  days in group I and II respectively. The values were statistically insignificant. During the present study it was observed that presentation is usually delayed by the owner unless prominent signs like muco-purulent discharge or loss of vision are noticed by the owner as observed by Moore (1990).

#### **5.3.5 Previous ocular disease**

80% of the presented dogs did not have any previous ocular disease, desmetocele was observed in 10% of dogs and maggot infestation was observed in 10% of dogs. Due to previous ocular disease or corneal damage the affected eye becomes more prone to damage because of irritation.

#### **5.3.6 Prior treatment before presentation**

Affected dogs had not received any previous treatment in 50% of the cases, topical ocular antibiotics and parental antibiotics had been given in 40% and 10% dogs respectively. Bacterial infections are usually associated with disease of the eyelids, cornea and conjunctiva due to loss of antimicrobial properties in tear film and previously as also observed by Whitley (2000) and Sirivasan and Nichols (2009). Although as most eyes with deficient tear production are no more infected with bacteria than are eyes with normal tears as reported by Williams *et al.* (2012).

#### **5.3.7 Vaccination Status**

Complete vaccination was followed in 40% cases and incomplete in 40% and not even started in 20% of the dogs (due to owner negligence). KCS could not be attributed to vaccination status in the present study.

### **5.4 Physiological Parameters**

All the recorded parameters were within the normal physiological range and not affected by KCS as no systemic problems were associated in them. Physiological

parameters showed a statistically non-significant variation on all the days of observation throughout the study period as also observed by Nagaraj, (2011).

## **5.5 Ophthalmic examination**

### **5.5.1 Eye affected**

Left eye (60%) was affected more frequently with KCS as compared to the right eye (40%). Affection in only one eye could be attributed to the fact that there is no direct anatomical connection between the both eyes and they are separate entities. Similar findings have been reported by Rani (2018) who observed that the left eye (51.72%) showed slightly higher occurrence of KCS in dogs in comparison to the right one. On the contrary Balicki *et al.* (2008) and Ramani *et al.* (2017) have reported higher incidence of involvement of both the eyes to the extent of 66-69% and 82.50% respectively. Kaswan *et al.* (1985) has reported that the immune- mediated, toxic and neurogenic form of KCS was primarily bilateral whereas traumatic one was unilateral in dogs.

### **5.5.2 Gross examination**

#### **5.5.2.1 Mucous membrane colour**

Mucous membrane congestion was seen in seven dogs (70%), no conjunctival changes were observed in 20%, paleness was shown by one dog (10%). Congestion occurred due to lack of lubrication and resultant friction by the eyelids and third eyelid or due to accumulation of inflammatory cells and blood vessels that infiltrate the anterior corneal stroma. In acute phase of KCS, the ocular surface appeared less bright and conjunctiva became extremely reddish and chemotic. Corneal epithelial cells exfoliate by the greater friction associated with blinking over a roughened, keratinized conjunctival epithelium exaggerate the symptoms. Similar observations have been noted by Berdoulay *et al.* (2005) who observed that corneal ulceration and ocular pain and epithelium undergoes squamous metaplasia due to KCS in dogs.

#### **5.5.2.2 Photophobia**

Photophobia decreased in all the dogs of both the groups as compared to the pre-treatment day 0 values. A statistical significant reduction in grades of photophobia was

observed from day 45 in group-I and 30<sup>th</sup> day in group- II. In the present study, due to ocular pain and irritation the eyes were sensitive to light, but on initiation of treatment, the triggering factor for photophobia reduced, as also observed by Sansom *et al.* (1995).

### **5.5.2.3 Rapidity of progression**

Increased onset of progression was seen in five cases (50%), acute in four cases (40%) and recurrence in one case (10%). Progression of disease results in chronic keratitis which leads to permanent corneal fibrosis or scarring and pigmentation which causes vision loss due to delay in the treatment. Bennett (1968) has also reported that KCS can be presented as either acute or chronic, wherein acute form, the affected eyes may be extremely painful and results in corneal ulceration, which is generally axial in position and progress very quickly to full thickness ulceration and globe rupture if not treated effectively. However, ulceration was not observed on day 0 in the ten presented cases.

### **5.5.3 Neuro-ophthalmic examination**

All the neuro-ophthalmic tests (Pupillary light reflex (PLR), Cotton ball test, Dazzle reflex test, Palpebral reflex, Menace reflex test, Visual placing postural reaction) showed good improvement on observations day 15, 30 and 45<sup>th</sup> in comparison to first day of presentation as cyclosporine and PDT surgery was observed to decrease inflammation and restore eye lubrication which improved the sensory and motor functions of eye as also reported by Moore, (2001) and Mitchell, (2011).

## **5.6 Diagnostic tests**

### **5.6.1 Schirmer tear test**

Schirmer tear test (STT-I) was a 'gold standard' test for diagnosing keratoconjunctivitis sicca (KCS) and conducted to detect the basal and reflex tears production in eyes without use of topical anaesthetic. During the present study, the test was performed to evaluate quantitative variations in aqueous component of precorneal tear film in the affected dogs. STT-I values were significantly decreased in keratoconjunctivitis sicca (KCS) affected dogs indicating decreased tear production. Mean

value of STT-I readings recorded in group-I was  $3.20 \pm 1.32$  mm/min and  $5.80 \pm 0.37$  mm/min in group-II dogs. The readings registered a increasing trend on all the observation days in comparison to day 0 value.

The precorneal tear film instability is due to both quantitative and qualitative deficiency in the lipid or mucin layers of tear film which is associated with blepharospasm, periocular dermatitis, corneal inflammation or even blinding (Aguirre *et al.*, 1971). KCS was occurring due to reduction of the aqueous layer in the pre-corneal tear film (PTF) resulted in desiccation of cornea and conjunctival inflammation, ocular pain, ulceration, melanosis, and vascularization but since, immunosuppressive drugs like cyclosporine, and use of lacromimetic drug like carboxymethyl cellulose were topically administered, an increase in STT readings throughout the observation period was noted as  $23.80 \pm 2.76$  mm/min in group-I and  $21.6 \pm 2.73$  in group-II. Increase in STT-I readings post-treatment has also been reported by Hamor *et al.* (2000) and Ofri (2009).

### 5.6.2 Schirmer tear test – II

STT-II was performed after the application of topical local anaesthetic and evaluated the basal tear secretion only (Hartley *et al.*, 2006). During the present study, mean values of STT-II readings recorded in group-I was  $0.80 \pm 0.20$ mm/min and  $0.60 \pm 0.24$ mm/min in group-II. The readings registered a increasing trend on all the observation days in comparison to day 0 and were statistically significant within the group from 15<sup>th</sup> day in both the groups. (Alkan *et al.*, 2004). The increase in values of Schirmer tear test-II was because of lacrimomimetic and lacrostimulant properties of cyclosporine which also decreased the elevated levels of inflammatory mediators causing increase in tear production in group-I and due to the lubricating effect of saliva in group-II.

Similar findings were reported by Hamor *et al.* (2000) and Berger and King (1998) wherein significant differences were found in STT-II values between dogs of different body weight who also observed that large dogs have higher basal tear production as compared to dogs of lesser body weight (Smith *et al.*, 1994 and Alkan *et al.*, 2004). Hakanson and Arnesson (1997) and Saito and Kotani (1999) have reported that STT-II values in dogs may be influenced by dogs breed, however, not much

difference in the tear secretions among the breeds affected with KCS was observed in the present study.

### **5.6.3 Tear film break up time**

The stability of the pre-corneal tear film (PTF) which depends on the lipid and mucin layers could be qualitatively evaluated with TFBUT which was found to be significantly decreased in KCS affected dogs. The values  $4.40 \pm 0.92$  in group-I and  $4.20 \pm 0.58$  in group-II showed an increasing trend from pre-treatment values throughout the observation period. The tear film instability in diseased eyes might be due to inflammation and loss of vascularization which was responsible for loss of goblet cells which is a primary source for mucin secretion in the eyes as also reported by Tseng *et al.* (1984) whereas, Moore *et al.* (1987) proposed a direct relationship existing between the degree of surface hydration (aqueous layer) and number of conjunctival goblet cells. Therefore, TFBUT is considered fundamental to diagnose the dry eye and is used to determine tear film instability (Giuliano and Moore, 2007).

## **5.7 Microbiological examination**

### **5.7.1 Antibiogram Pattern**

Antibiogram pattern of seven antibiotics were tested and gentamicin and moxifloxacin were used as topical drugs in the present study as per their more comparative sensitivity. Antibiotics decreased the bacterial infections which is responsible for ocular signs reduced the ocular bacterial infections because bacterial infections are usually associated with diseases of eyelids, cornea and conjunctiva due to loss of antimicrobial properties in tear film. The efficacy of ciprofloxacin, moxifloxacin and norfloxacin (Whitely, 2000) and gentamicin (Bharathi, 2009 and Ramani *et al.*, 2013) as topical ophthalmic antibiotics in the management of ocular bacterial infections has been suggested in various studies.

In the present study, gentamicin and moxifloxacin proved to be highly effective and superior in the treatment of KCS due to their capability of low bacterial resistance.

## **5.8 Biochemical analysis**

Analysis of biochemical parameters on day 0, 15, 30 and 45 revealed that all values in both group I and II were within normal physiological range and were

statistically non-significant as all the similar findings were observed by Hendrix *et al.* (2011) and John *et al.* (2018). All the dogs presented in the present investigation, all the dogs presented were clinically healthy with no systemic affections were associated with them who observed that there are several systemic infectious diseases including viral, bacterial, fungal and parasitic diseases that cause adverse changes in lacrimal gland. However, no such changes were not seen during the study period.

## **5.9 Haematological parameters**

All the values of haematological parameters in both groups estimated on day 0 were within the normal reference range and non-significant statistically.

Thus from the present investigation it can be concluded that the haematological parameters were unaltered due to the KCS encountered in dogs because they didn't reflect any systemic reaction. The values remained within the normal physiological limits for the whole period of observation. The findings of the study were in conjunction with Williams (2010) and Nagaraj (2011) who recorded normal haematological values in KCS affected dogs.

## **5.10 Management of KCS**

### **5.10.1 Medicinal therapy**

During the study, the KCS affected dogs (n=10) were randomly divided into two groups of five dogs each. In group I, the therapeutic efficacy of cyclosporine against KCS was judged based on the improvement in clinico-ophthalmic signs and ocular surface test values returned to the normal level, from day 15 onwards.

Dogs belonging to group I were administered with topical application of cyclosporine ophthalmic ointment (2mg/gm) b.i.d, q 12 hr for 45 days, methylcellulose eye drops q.i.d, q 4 hr Gatifloxacin/ Moxifloxacin drops t.i.d for 2 weeks. The dogs in the group showed improvement in clinico- ophthalmic signs within 45 days of treatment. The increase in STT (I & II) and TFBUT were found significant on post-treatment. The regimen showed good therapeutic efficacy (100%) in all dogs.

Cyclosporine (CsA) is a lipophilic naturally occurring fungal metabolite (Matsuda and Koyasu, 2000) which exhibits lacrimostimulant and lacrimomimetic properties and significantly improves STT values in KCS affected dogs. It blocks JNK (C- Jun N-terminal kinases) and p38 signaling pathways and stops the aggression of lachrymal gland to stop inflammatory corneal and conjunctival lesions as also observed by Moore (2001), Tilley and Smith (2015), Hendrix *et al.* (2011), Nagaraj (2011), Matheis *et al.* (2012) and Izci *et al.* (2015).

During the present study, methyl cellulose ophthalmic drops were used for two weeks as post-treatment which helped to lubricate the ocular surface and remove debris, and give relief to the tissues, cornea and conjunctiva and reduce the elevated levels of inflammatory mediators as also reported by Nagaraj (2011). Hydroxypropyl and carboxy methyl cellulose could also be used as lubricants and tear substitutes which stabilized the retention of tear film as reported by Dodi *et al.* (2009). Gentamicin or Moxifloxacin antibiotics were used for two weeks in the present study in both groups as topical antibiotics during the first phase of the therapy to counteract the secondary bacterial infections that are common in KCS. Whitely (2000) and Ramani *et al.* (2013) have also reported the efficacy of moxifloxacin and gantamicin respectively in KCS affected dogs.

### **5.10.2 Surgical management**

In group-II (n=5), dogs of either sex affected with KCS were included in the clinical study. The ophthalmic examination was easily performed in all the dogs without any chemical restraint.

#### **5.10.2.1 Anaesthesia**

All the surgical manipulations were done under atropine @ 0.04 mg/kg b.wt., xylazine hydrochloride @ 2 mg/kg b.wt., ketamine hydrochloride @ 10 mg/kg b.wt. and diazepam @ 0.14 mg/kg b.wt and ketamine HCL @ 3.5 mg/kg b.wt combination (1:25w/w). This anaesthesia provided adequate analgesia and kept the eye central during the entire procedure and was not associated with any anaesthetic complications were observed as also reported by Ozgenel *et al.* (2000) using the same anesthetic protocol.

### 5.10.2.2 Surgical technique

Restraint of all the affected animals in lateral recumbency with the affected eye up provided adequate exposure to the eye. The surgery involved re-routing the parotid duct into the conjunctiva which provided saliva to the eye and lubricated the ocular surface. Parotid duct transposition was easily performed in all the five cases. Parotid papilla was cannulated by using 24 gauge intravenous catheter for identification and manipulation of the duct and was found appropriate to catheterise the parotid duct. Mitchell (2011) has suggested the use of 2-0 monofilament nylon or polydioxane (PD S) to identify the duct. The 6/0 polyglactin suture was found to be appropriate for suturing the parotid papilla into the ventral conjunctival sac. On the basis of clinical findings, STT and TFBUT results, PDT improved the ocular comfort, delayed progression of visual impairment and improved vision however, minor surgical complications were observed. Williams (2002), Rhodes *et al.* (2012), Schilke and Sapienza (2012), Lewin (2014) and Dodi (2015) have also opined that PDT is the most suitable surgical treatment for restoring ocular health in medically refractive cases of KCS.

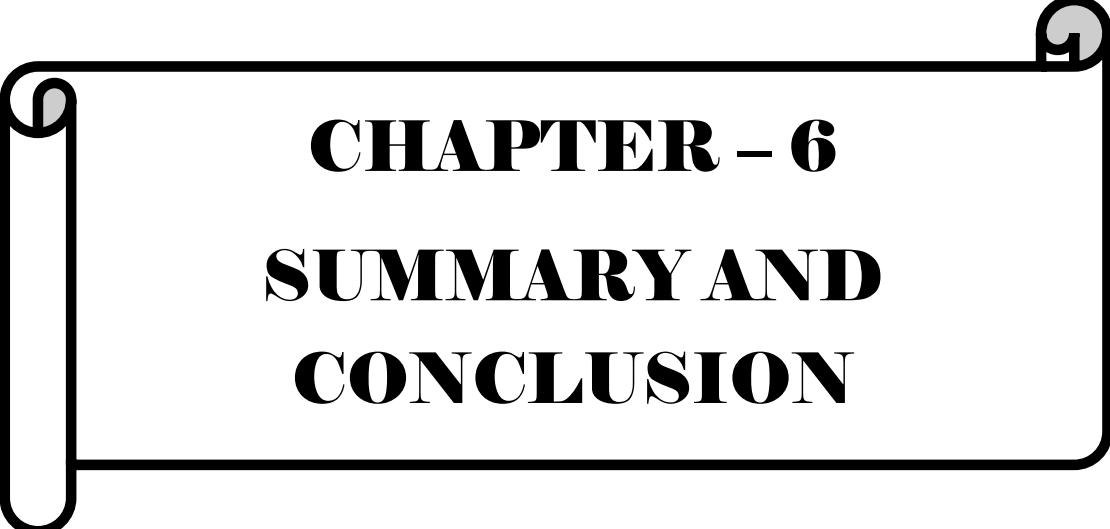
### 5.10.2.3 Post-operative treatment

In the present study, flurbiprofen drops b.i.d. and methylcellulose eye drops t.i.d. were used post-operatively up to two weeks which reduced corneal irritation and oedema. Mitchell (2011) have also suggested use of methylcellulose eye drops t.i.d. until the animal started eating properly in PDT cases. Moxifloxacin and Gentamicin drops were used topically and observed to be effective antibiotics to prevent bacterial infections as represented by reduced congestion. Therefore, changes in demeanor, pawing/face rubbing were not recorded in any dog. During the post-operative period, the moisture of the eye was monitored by visualising the degree of wetness of the eye at the time of feeding observed by owner in group-II and by performing schirmer tear test on follow up days in both the groups. Elizabethan collar was advised in all the dogs post-operatively, which was effective to prevent self mutilation. Importance of use of Elizabethan collar has been stated by Sanchez *et al.* (2007). The owners were advised to give meals in small quantities frequently in order to establish a continuous supply of secretion until skin sutures were removed on 10<sup>th</sup> day in group-II.

### 5.11 Post-operative outcome, complications and their management

Re-evaluation of all the dogs at every fifteen day interval up to 45 day, showed improvement in ocular health of both the groups as confirmed by increase in the STT I, II and TFBUT values. Dogs of group-II showed a better percentage improvement in comparison to group-I dogs in respect of STT-II (1600%) and TFBUT (176.19%) readings, however, STT-I readings showed a higher percent improvement was in group-I as compared to group II dogs. Cyclosporine has lacrimogenic activities through its immunomodulatory effects, reducing or preventing cytokine production by lymphocytes and saliva contains enzymes such as amylase which regulates the stimulation of tears, thereby showing a drastic increase in tear film post treatment as also reported by Williams (2018).

In group-II, despite the relatively high success rate of PDT, minor complications included stenosis of duct in two dogs (40%), corneal ulceration (10%) and irritation in one dog each (10%). Irritation by the suture end resulted in corneal ulceration in one dog on 45<sup>th</sup> day. Rhodes *et al.* (2012) has also observed that corneal ulceration resulted from incorrect placement of the parotid duct papilla or by the sutures within the ventral conjunctival fornix. The suture was removed and the ulceration resolved by medicinal treatment alone. Severe intolerance to saliva leads to irritation and is observed to be a most serious complication as also observed by Dodi (2015) in his study. To minimize the corneal irritation, the long term topical antibiotic treatment was advised post-operatively to the owners. Reduced application of topical medication was one factor which was likely to have favourably influenced client satisfaction with the PDT procedure. Results of both the groups indicated that owners perceived significant improvements in the ocular comfort, rubbing less and daily maintenance of dog with fewer topical medication.



**CHAPTER – 6**  
**SUMMARY AND**  
**CONCLUSION**

## CHAPTER VI

### SUMMARY AND CONCLUSIONS

The present study was conducted on ten dogs of either sex affected with keratoconjunctivitis sicca of age varying from seven month to 10 years and weighing 5 kg to 42.3 kgs, presented to the Teaching Veterinary Clinical Complex, F.V.Sc. & A.H., R.S. Pura, Jammu during the period from August 2018- June 2019.

During the present investigation the prevalence of canine keratoconjunctivitis sicca (KCS) was found to be 34.92% out of the ocular cases presented based on STT-I reading  $< 5$  mm/ min. KCS was observed to be higher in brachycephalic breeds, most commonly in pugs. The highest incidence rate of KCS was recorded in middle to old aged dogs and predominantly observed in male dogs (70%).

Chief complaint reported by the owner included redness, blepharospasm, mucoid to mucopurulent ocular discharge with a history of unknown cause. During the study on visual acuity in KCS affected dogs, 50% of the cases showed blindness. Mean duration of KCS damage on presentation were  $16.4 \pm 5.60$  and  $16.0 \pm 3.78$  in group I and II respectively. In most of the affected cases the ocular discharge was muco-purulent (50%). Non-significant variation in physiological parameters was observed in all the dogs of both the groups. Ophthalmic examination revealed that the left eye (60%) was affected slightly more than the right eye (40%). Mucous membrane congestion was observed in 70% of the affected dogs with decrease in photophobia as compared to the pre-treatment day 0 values. A statistical significant decline in grades of photophobia throughout the study period was observed.

Neuro-ophthalmic tests showed improvement in both the groups post treatment. Schirmer tear test- I (STT-I) readings recorded post-treatment in all affected dogs showed increasing STT-I values, in comparison to pre-treatment values. STT-I & II values were statistically significant from post- operative day 15 till 45 day in both the groups.

During the present investigation, a decrease in tear film breakup time (TFBUT) in dogs of both groups was observed on day 0. The values increased post treatment and were significant from day 15 till 45 in group I and II respectively.

Antibiogram pattern of seven antibiotics was carried out and Gentamicin and Moxifloxacin antibiotics were shown to have good effectiveness against KCS in dogs. Blood glucose, serum albumin, serum globulin and total protein were estimated in all the affected dogs on day 0, 15, 30 and 45. The values in both the groups were statistically non-significant and within normal reference range. Haematological parameters estimated on day 0 in both groups were non-significant and within the normal reference range.

Topical application of cyclosporine ophthalmic ointment (2mg/gm) b.i.d, q 12 hr was used in the entire study period, methylcellulose eye drops q.i.d, q 4 hr and flurr eye drops b.i.d and Gentamicin/ Moxifloxacin drops t.i.d for 2 weeks in group-I (n=5) were administered and found suitable in treating canine Keratoconjunctivitis sicca (KCS). The dogs in the group-I showed improvement in clinico- ophthalmic signs based on ocular surface tests and the therapeutic efficacy was found to be 100%.

Parotid duct transposition was performed in group-II (n=5). Surgical manipulations were done under proper anaesthetic protocol which provided adequate analgesia and kept the eye central during the entire surgical procedure. The surgery involved re-routing the parotid salivary duct from the parotid papilla in the mouth to the ventral conjunctival sac. Parotid papilla was cannulated by using 24 gauge intravenous catheter for identification and manipulation of the duct and was found appropriate to catheterise the parotid duct, blunt dissection of parotid duct was performed and duct was sutured into the ventral conjunctival sac using 6/0 polygalactin suture. Post-operative medication used was flurbiprofen drops b.i.d., methylcellulose eye drops t.i.d. and moxifloxacin drops t.i.d. for one week in group-II to reduced corneal irritation, edema, blepharitis and bacterial infection. The patency of duct was re-evaluated on post-observation days by placing the drops of atropine 1% on the tongue and response was observed as the saliva was emerging in the treated eye. Test results of STT-II and TFBUT in group II showed better improvement percentage as compared to dogs of group I. However, STT-I improvement percentage was more in dogs of group I.

On the basis of the results, the following conclusions were drawn from the present study:

1. 34.92% of dogs out of the ocular affections were affected with KCS during the study period of August 2018 to June 2019.
2. KCS is higher in brachycephalic breeds, most commonly in pugs and middle to old aged dogs. Frequent muco-purulent discharge was seen in affected cases and male dogs were affected more.
3. Gentamicin and Moxifloxacin were effective antibiotics against KCS in dogs.
4. Schirmer tear test (STT) and Tear film break- up time (TBUT) were easy and effective diagnostic tests to measure the tear production and lipid and mucin deficiencies respectively in KCS cases of dogs.
5. Medication with cyclosporine improved the vision, decreased the conjunctivitis, mucous discharge and significantly improved the precorneal tear film. The therapeutic efficacy was found to be 100% and is an easy option than surgery.
6. PDT was a successful procedure based on the improvement observed and reduced the need of the frequent topical medication. However, it was associated with minor complications.

PDT is suggested as a treatment option for restoring the ocular surface health in KCS cases in dogs especially when owner compliance is poor.

Therefore, it is concluded that treatment with both cyclosporine and Parotid duct transposition are suitable in treating canine kerato-conjunctivitis sicca (KCS) as all the dogs showed similar clinico-ophthalmic improvement from the condition and the treatment efficacy was found to be 100%. However, in cyclosporine group-I, life-long therapy is indicated for KCS in dogs and PDT provides adequate secretions to keep the cornea moist without the need for post-medication and is a suitable alternative in non-compliant clients.



**REFERENCES**

## REFERENCES

- Aguirre, G.D., Rubin, L.F. and Harvey, C.E. 1971. Keratoconjunctivitis sicca in dogs. *Journal of the American Veterinary Medical Association*, **158**(9): 1566–1579.
- Alkan, F., İzci, C., Tepeli, C. and Koc, Y. 2004. Evaluation of the Schirmer Tear Test in two Turkish breeds of Shepherd dogs. *Revue de medecine veterinaire*, **155**(2): 67-70.
- Amol, P. E. 2016. Studies on the incidence, diagnosis and management of different ocular affections in brachycephalic dogs (Doctoral dissertation, Anand Agricultural University, Anand).
- Balicki, I., Radziejewski, K. and Silmanowicz, P. 2008. Studies on keratoconjunctivitis sicca incidence in crossbred dogs. *Polish Journal of Veterinary Sciences*, **11**(4): 353-358.
- Barabino, S., Chen, W. and Dana, M. R. 2004. Tear film and ocular surface tests in animal models of dry eye: uses and limitations. *Experimental Eye Research*, **79**(5): 613-621.
- Barnett, K. C. and Sansom, J. 1985. Dry eye in the dog and its treatment. *Transactions of the Ophthalmological Societies of the United Kingdom*, **104**: 462-466.
- Barnett, K. C. and Sansom, J. 1987. Diagnosis and treatment of keratoconjunctivitis sicca in the dog. *The Veterinary Record*, **120**(14): 340-345.
- Behrens, A., Doyle, J. J., Stern, L., Chuck, R. S., McDonnell, P. J., Azar, D. T. and Lemp, M. A. 2006. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. *Cornea*, **25**(8): 900-907.
- Bennett, J. E. 1968. The management of total xerophthalmia. *Transactions of the American Ophthalmological Society*, **66**: 503.

- Berdoulay, A., English, R. V. and Nadelstein, B. 2005. Effect of topical 0.02% tacrolimus aqueous suspension on tear production in dogs with keratoconjunctivitis sicca. *Veterinary Ophthalmology*, **8**(4): 225-232.
- Berger, S. L. and King, V. L. 1998. The fluctuation of tear production in the dog. *Journal of the American Animal Hospital Association*, **34**(1): 79-83.
- Berger, S. L., Scagliotti, R. H., Lund, E. M., Berta, G., Trotta, A., Fusconi, A. and Morini, S. 1995. A quantitative study of the effects of Tribissen on canine tear production. *Journal of the American Animal Hospital Association*, **31**(3): 236-241.
- Bharathi, S. 2009. Clinical study on ocular diseases of surgical importance in dogs (Doctoral dissertation, Sri Venkateswara Veterinary University, Tirupati).
- Bron, A. J., Evans, V. E. and Smith, J. A. 2003. Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea*, **22**(7): 640-650.
- Carrington, S. D., Bedford, P. G., Guillon, J. P. and Woodward, E. G. 1989. Biomicroscopy of the tear film: the tear film of the pekingese dog. *The Veterinary Record*, **124**(13): 323-328.
- Cher, I. 2003. Blink-related microtrauma: when the ocular surface harms itself. *Clinical and experimental Ophthalmology*, **31**(3): 183-190.
- Conrady, C. D., Joos, Z. P. and Patel, B. C. 2016. The lacrimal gland and its role in dry eye. *Journal of Ophthalmology*, pp 1-11.
- Cullen, C. L., Lim, C. and Sykes, J. 2005. Tear film breakup times in young healthy cats before and after anesthesia. *Veterinary Ophthalmology*, **8**(3): 159-165.
- Davidson, H. J. and Kuonen, V. J. 2004. The tear film and ocular mucins. *Veterinary Ophthalmology*, **7**(2): 71-77.

- De Almeida, D.E., Roveratti, C., Brito, F.L., Godoy, G.S., Duque, J.C., Bechara, G.H., and Laus, J.L. 2009. Conjunctival effects of canine distemper virus-induced keratoconjunctivitis sicca. *Veterinary Ophthalmology*, **12**(4), 211-215.
- Dodi, P. L. 2015. Immune-mediated keratoconjunctivitis sicca in dogs: current perspectives on management. *Veterinary Medicine: Research and Reports*, **6**: 341.
- Dodi, P. L., Zanotti, C., Rossi, S., and Aloe, L. 2009. Tear level of nerve growth factor in normal dogs. *Acta Ophthalmologica*, **87**.
- Doughty, M. J. 2013. Rose bengal staining as an assessment of ocular surface damage and recovery in dry eye disease—a review. *Contact Lens and Anterior Eye*, **36**(6): 272-280.
- Dugan, S. J., Severin, G. A., Hungerford, L. L., Whiteley, H. E. and Roberts, S. M. 1992. Clinical and histologic evaluation of the prolapsed third eyelid gland in dogs. *Journal of the American Veterinary Medical Association*, **201**(12): 1861-1867.
- Eubanks, D. L. and Woodruff, K. A. 2010. The basics of saliva. *Journal Veterinary Dentistry*, **27**(4): 266-267.
- Evans., H. E. and De Lahunta, A. 2013. *Miller's anatomy of the dog-E-Book*. Elsevier Health Sciences. **pp**: 1110-114.
- Featherstone, H.J. and Heinrich, C.L. (2013). Ophthalmic examination and diagnostics. *In*: Gelatt, K.N., Gilger, B.C. and Kern, T.J. (eds.). *Veterinary Ophthalmology. 5th edn*. John Wiley and Sons, Inc. **pp**: 533–702.
- Gao, J., Gelber-Schwalb, T. A., Addeo, J. V. and Stern, M. E. 1998. Apoptosis in the lacrimal gland and conjunctiva of dry eye dogs. *In Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2* pp: 453-460.
- Gelatt, K. N., and Brooks, D. E. 1999. *In* Gelatt KN (editor): *Veterinary Ophthalmology*.
- Gelatt, K. N., Bernhard, M. S. and Brian, C. G. 2011. Vitreoretinal surgery. *Veterinary Ophthalmic Surgery. St. Louis: Elsevier Saunders*: 357-87.

- Gelatt, K.N. 2000. Diseases and surgery of the canine eyelids. In: *Essentials of Veterinary Ophthalmology*, Lippincott Williams and Wilkins, Philadelphia. pp: 67-72.
- Gelatt, K.N., Whitley, R. D. and Samuelson, D. A. 1985: Ocular manifestations of viral diseases in small animals. *Compendium on Continuing Education*, **7**, pp: 968-977.
- Gilger, B. C. and Allen, J. B. 1998. Cyclosporine A in veterinary ophthalmology. *Veterinary Ophthalmology*, **1**(4): 181.
- Gipson, I. K., Yankauckas, M., Spurr-Michaud, S. J., Tisdale, A. S. and Rinehart, W. 1992. Characteristics of a glycoprotein in the ocular surface glycocalyx. *Investigative Ophthalmology and Visual Science*, **33**(1): 218-227.
- Giuliano, E. A., and Moore, C. P. 2007. Diseases and surgery of the lacrimal secretory system. *Veterinary Ophthalmology*, **4**: 633-661.
- Grahn, B. H., and Storey, E. S. 2004. Lacrimomimetics and lacrimostimulants. *Veterinary Clinical North American Small Animal Practice*, **34**(3): 739-53.
- Hakanson, N. W. and Arnesson, K. 1997. Temporal variation in tear production in normal beagle dogs as determined by Schirmer tear test. *Veterinary and Comparative Ophthalmology (USA)*.
- Hamor, R. E., Roberts, S. M., Severin, G. A., and Chavkin, M. J. 2000. Evaluation of results for Schirmer tear tests conducted with and without application of a topical anesthetic in clinically normal dogs of 5 breeds. *American Journal of Veterinary Research*, **61**(11): 1422-1425.
- Hartley, C., Williams, D. L. and Adams, V. J. 2006. Effect of age, gender, weight, and time of day on tear production in normal dogs. *Veterinary Ophthalmology*, **9**(1): 53-57.
- Helper, L. C. 1970. Effect of lacrimal gland removal on the conjunctiva and cornea of the dog. *Journal of American Veterinary Medical Association Journal*, 41-43.

- Helper, L. C. 1996. The tear film in the dog. Causes and treatment of diseases associated with overproduction and underproduction of tears. *Animal Eye Research*, **15**: 5-11.
- Hendrix, D. V., Adkins, E. A., Ward, D. A., Stuffle, J. and Skorobohach, B. 2011. An investigation comparing the efficacy of topical ocular application of tacrolimus and cyclosporine in dogs. *Veterinary Medicine International*, 1-5.
- Herrera, H. D., Weichsler, N., Gómez, J. R. and De Jalón, J. A. G. 2007. Severe, unilateral, unresponsive keratoconjunctivitis sicca in 16 juvenile Yorkshire Terriers. *Veterinary Ophthalmology*, **10**(5): 285-288.
- Herring, I. P., Pickett, J. P., Champagne, E. S. and Marini, M. 2000. Evaluation of aqueous tear production in dogs following general anesthesia. *Journal of the American Animal Hospital Association*, **36**(5): 427-430..
- Hirayama, M., Ogawa, M., Oshima, M., Sekine, Y., Ishida, K., Yamashita, K. and Tsuji, T. 2013. Functional lacrimal gland regeneration by transplantation of a bioengineered organ germ. *Nature Communications*, **4**: 2497.
- Hollingsworth, S. R., Canton, D. D., Buyukmihci, N. C. and Farver, T. B. 1992. Effect of topically administered atropine on tear production in dogs. *Journal of American Veterinary Association*, **200**(10):1-5.
- Izci, C., Celik, I., Alkan, F., Erol, M. and Sur, E. 2015. Clinical and light microscopic studies of the conjunctival tissues of dogs with bilateral keratoconjunctivitis sicca before and after treatment with topical 2% cyclosporine. *Biotechnic and Histochemistry*, **90**(3): 223-230.
- Jabs, D. A., Lee, B., Whittum-Hudson, J. and Prendergast, R. A. 2001. The role of Fas-Fas ligand-mediated apoptosis in autoimmune lacrimal gland disease in MRL/MpJ mice. *Investigative Ophthalmology and Visual Science*, **42**(2): 399-401.

- Jain, N.C. 1986. Schalm's Veterinary Haematology, 4<sup>th</sup> ed. pp. 431-486. Lea and Febiger, Philadelphia.
- John, C., Gopinathan, A., Singh, K., Sharma, P., Sowbharenaya, C. and Sarangom, S.B. 2018. Clinical evaluation of topical tacrolimus ointment usage in different stages of Keratoconjunctivitis sicca in dogs. *Turkish Journal of Veterinary and Animal Sciences*, **42**(4): 259-268.
- Kaswan, R. L. and Salisbury, M. A. 1990. A new perspective on canine keratoconjunctivitis sicca: treatment with ophthalmic cyclosporine. *Veterinary Clinics of North America: Small animal practice*, **20**(3): 583-613.
- Kaswan, R. L., Martin, C. L. and Dawe, D. L. 1985. Keratoconjunctivitis sicca: immunological evaluation of 62 canine cases. *American Journal of Veterinary Research*, **46**(2): 376-383.
- Kaswan, R.L., Salisbury, M.A. and Ward, D.A. 1989. Spontaneous canine keratoconjunctivitis sicca. A useful model for human keratoconjunctivitis sicca: treatment with cyclosporine eye drops. *Archives of Ophthalmology*, **107**(8): 1210-16.
- Krecny, M., Tichy, A., Rushton, J., and Nell, B. 2015. A retrospective survey of ocular abnormalities in pugs: 130 cases. *Journal of Small Animal Practice*, **56**(2): 96-102.
- Kunert, K. S., Tisdale, A. S. and Gipson, I. K. 2002. Goblet cell numbers and epithelial proliferation in the conjunctiva of patients with dry eye syndrome treated with cyclosporine. *Archives of Ophthalmology*, **120**(3): 330-337.
- Lavignette, A. M. 1966. Keratoconjunctivitis sicca in a dog treated by transposition of the parotid salivary duct. *Journal of the American Veterinary Medical Association*, **148**(7): 778.
- Lewin, A. 2014. Keratoconjunctivitis sicca in dogs: causes, diagnosis and treatment. *Veterinary Times*. **6**: 16-17.

- Maggs, D. J. 2008. Basic diagnostic techniques. *Slatter's Fundamentals of Veterinary Ophthalmology*, **4**: 81-106.
- Marsh, P. and Pflugfelder, S. C. 1999. Topical nonpreserved methylprednisolone therapy for keratoconjunctivitis sicca in Sjögren syndrome. *Ophthalmology*, **106**(4): 811-816.
- Matheis, F. L., Walser-Reinhardt, L. and Spiess, B. M. 2012. Canine neurogenic keratoconjunctivitis sicca: 11 cases (2006–2010). *Veterinary Ophthalmology*, **15**(4): 288-290.
- Matsuda, S. and Koyasu, S. 2000. Mechanisms of action of cyclosporine. *Immunopharmacology*, **47**(2-3): 119-125.
- Miller, P. E. 2008. Lacrimal system. In: Maggs, D.J., Miller, P.E. and Ofri. R. editors. *Slatter's Fundamentals of Veterinary Ophthalmology*. 4th ed. St Louis: Saunders Elsevier, 166–171.
- Mitchell, N. 2011. Approach to ocular examination in small animals. *In Practice*, **33**(4), 146-154.
- Moore, C. P. 1990. Qualitative tear film disease. *Veterinary Clinics of North America: Small Animal Practice*, **20**(3): 565-581.
- Moore, C. P. 1999. Diseases and surgery of the lacrimal secretory system. *Veterinary Ophthalmology*, 583-607.
- Moore, C. P., and Collier, L. L. 1990. Ocular surface disease associated with loss of conjunctival goblet cells in dogs. *Journal of the American Animal Hospital Association*, **26**(5): 458-466.
- Moore, C. P., Wilsman, N. J., Nordheim, E. V., Majors, L. J., and Collier, L. L. 1987. Density and distribution of canine conjunctival goblet cells. *Investigative Ophthalmology and Visual Science*, **28**(12): 1925-1932.

- Moore, P. A. 2001. Examination techniques and interpretation of ophthalmic findings. *Clinical Techniques in Small Animal Practice*, **16**(1):1-12.
- Morgan, R. V., and Abrams, K. L. 1991. Topical administration of cyclosporine for treatment of keratoconjunctivitis sicca in dogs. *Journal of the American Veterinary Medical Association*, **199**(8): 1043-1046.
- Nagaraj, P. 2011. Clinical and diagnostic studies on certain ophthalmic conditions in dogs and their therapeutic management. (Doctoral dissertation, Sri Venkateswara Veterinary University, Tirupati-517 502, AP).
- Ofri, R. 2009. Clinical evaluation of pimecrolimus eye drops for treatment of canine keratoconjunctivitis sicca: A comparison with cyclosporine A. *The Veterinary Journal*, **179**(1): 70-77.
- Olivero, D. K., Davidson, M. G., English, R. V., Nasisse, M. P., Jamieson, V. E. and Gerig, T. M. 1991. Clinical evaluation of 1% cyclosporine for topical treatment of keratoconjunctivitis sicca in dogs. *Journal of the American Veterinary Medical Association*, **199**(8): 1039-1042.
- Ozgenel, G. Y., Ozcan, M. and Kahveci, Z. (2000). An experimental study of bilateral repositioning of the Stenses's duct orifices with autologous vein and artery grafts in dogs. *British Journal of Plastic Surgery*, **53**(2): 106-108.
- Pal, S., Sadhu, A. S., Patra, S. and Mukherjea, K. K. 2008. Histological vis-a-vis biochemical assessment on the toxic level and antineoplastic efficacy of a synthetic drug Pt-ATP on experimental animal models. *Journal of Experimental and Clinical Cancer Research*, **27**(1): 68.
- Pierce, V. and Williams, D. 2006. Determination of Schirmer Tear test values in 1000 dogs. BSAVA Abstract.
- Ramani, C., Krishnaveni, N., Shafiuzama, M. and George. R.S. 2017. Incidence of keratoconjunctivitis sicca in dogs. *Indian Journal of Canine Practice*, **9**(1): 53:55

- Ramani, C., Rambabu, K., D'Souza, N. J., Vairamuthu, S., Subapriya, S., and William, B. J. 2013. Surgical bacteriology and grading of corneal ulcers in dogs a retrospective study in 24 dogs. *Indian Journal of Canine Practice*, **5**(1): 136-138.
- Rani, S. S. 2018. Diagnosis and therapeutic management of keratoconjunctivitis sicca in dogs (Doctoral dissertation, PVNR TVU).
- Rhodes, M., Heinrich, C., Featherstone, H., Braus, B., Manning, S., Cripps, P. J., and Renwick, P. 2012. Parotid duct transposition in dogs: a retrospective review of 92 eyes from 1999 to 2009. *Veterinary Ophthalmology*, **15**(4): 213-222.
- Saito, A. and Kotani, T. 1999. Tear production in dogs with epiphora and corneal epitheliopathy. *Veterinary Ophthalmology*, **2**(3): 173-178.
- Saito, A. and Kotani, T. 2001. Estimation of lacrimal level and testing methods on normal beagles. *Veterinary Ophthalmology*, **4**(1): 7-11.
- Sakai, T. 1989. Major ocular glands (Harderian gland and lacrimal gland) of the musk shrew (*Suncus murinus*) with a review on the comparative anatomy and histology of the mammalian lacrimal glands. *Journal of Morphology*, **201**(1): 39-57.
- Salisbury, M.A., Kaswan, R.L. and Brown, J. 1995. Microorganisms isolated from the corneal surface before and during topical cyclosporine treatment in dogs with keratoconjunctivitis sicca. *American Journal of Veterinary Research*, **56**(7): 880-884.
- Sanchez, R. F., Innocent, G., Mould, J. and Billson, F. M. 2007. Canine keratoconjunctivitis sicca: disease trends in a review of 229 cases. *Journal of Small Animal Practice*, **48**(4): 211-217.
- Sansom, J., Barnett, K. C., Neumann, W., Schulte-Neumann, A., Clerc, B., Jegou, J. P., and Weingarten, A. 1995. Treatment of keratoconjunctivitis sicca in dogs with cyclosporine ophthalmic ointment: a European clinical field trial. *The Veterinary Record*, **137**(20): 504-507.

- Sapienza, J. S., Mayordomo, A. and Beyer, A. M. 2014. Suture anchor placement technique around the insertion of the ventral rectus muscle for the replacement of the prolapsed gland of the third eyelid in dogs: 100 dogs. *Veterinary Ophthalmology*, **17**(2): 81-86.
- Schilke, H. K. and Sapienza, J. S. 2012. Partial ligation of the transposed parotid duct at the level of the parotid gland for excessive salivary secretions. *Veterinary Ophthalmology*, **15**(6): 411-416.
- Schirmer, O. 1903. Studies on the physiology and pathology of tear secretion and tear drainage. *Graefe's Archive for Clinical and Experimental Ophthalmology*, **56** (2): 197-291.
- Schmidt, G., Magrane, W. G. and Helper, L. C. 1970. Parotid duct transposition: a follow-up study of 60 eyes. *Journal of American Animal Hospital Association*, **6**: 235-41.
- Schreiber, S. L. and Crabtree, G. R. 1992. The mechanism of action of cyclosporin A and FK506. *Immunology Today*, **13**(4): 136-142.
- Scotti, S., Klein, A., Vanore, M., Hidalgo, A., Fayolle, P. and Moissonnier, P. 2007. A new surgical method for the control of the epiphora in dogs: modified parotid duct transposition. *Journal of Small Animal Practice*, **48**(5): 279-282.
- Sirivasan, S. and Nichols, K. K. (2009). "Collecting tear osmolarity measurement in the diagnosis of dry eye." *Expert Review of Ophthalmology*, **4**(5): 451-453.
- Slatter, D. H. 2001. Basic diagnostic tests. In: Slatter, D. H. (ed). *Fundamentals of Veterinary Ophthalmology*. 3<sup>rd</sup> edn. Saunders, Saint Louis, Missouri, U.S.A., pp 85- 123.
- Smith, E. M., Buyukmihci, N. C. and Farver, T. B. 1994. Effect of topical pilocarpine treatment on tear production in dogs. *Journal of American Veterinary Medical Association*, **205** (9):1-5.

- Stern, M. E., Gao, J., Siemasko, K. F., Beuerman, R. W. and Pflugfelder, S. C. 2004. The role of the lacrimal functional unit in the pathophysiology of dry eye. *Experimental Eye Research*, **78**(3): 409-416.
- Stevenson, D., Tauber, J., Reis, B. L. and Cyclosporin A Phase 2 Study Group. 2000. Efficacy and safety of cyclosporin A ophthalmic emulsion in the treatment of moderate-to-severe dry eye disease: a dose-ranging, randomized trial. *Ophthalmology*, **107**(5): 967-974.
- Strubble, D. T. 1991. Ophthalmic examination and Diagnostic procedures. In: Gelatt, K. N (ed). *Veterinary Ophthalmology*. 3<sup>rd</sup> edn. pp 427-430. Lippincott, William and Wilkins, Baltimore, Maryland, U.S.A.
- Thompson, S., Whiting, R. E., Kardon, R. H., Stone, E. M., and Narfstrom, K. 2010. Effects of hereditary retinal degeneration due to a CEP290 mutation on the feline pupillary light reflex. *Veterinary Ophthalmology*, **13**(3): 151-157.
- Tilley, L. P., and Smith Jr, F. W. 2015. *Blackwell's five-minute Veterinary consult: canine and feline*. John Wiley and Sons.
- Tseng, S. C., Hirst, L. W., Maumenee, A. E., Kenyon, K. R., Sun, T. T., and Green, W. R. 1984. Possible mechanisms for the loss of goblet cells in mucin-deficient disorders. *Ophthalmology*, **91**(6): 545-552.
- Turner, S. M. 2008. Cornea. In: Turner, S.M. (editor). *Small Animal Ophthalmology*. First edition, Saunders- Elsevier, China. P 121-197.
- Utine, C. A., Stern, M. and Akpek, E. K. 2010. Clinical review: topical ophthalmic use of cyclosporin A. *Ocular Immunology and Inflammation*, **18**(5): 352-361.
- Whitley, R. D. 2000. Canine and Feline Primary Ocular Bacterial Infections. *Veterinary Clinics: Small Animal Practice*, **30**(5): 1151-1167.
- Wilcock, B. 2008. General pathology of the eye. *Slatter's Fundamentals of Veterinary Ophthalmology*, **4**: 62-80.

- Williams, D. 2018. Canine Keratoconjunctivitis Sicca: Current Concepts in Diagnosis and Treatment. *Journal of Clinical Ophthalmology and Optometry*, **2**(1): 101.
- Williams, D. and Hewitt, H. 2017. Tear ferning in normal dogs and dogs with keratoconjunctivitis sicca. *Open Veterinary Journal*, **7**(3): 268-272.
- Williams, D. L. 2002. Use of punctal occlusion in the treatment of canine keratoconjunctivitis sicca. *Journal of Small Animal Practice*, **43**(11): 478-481.
- Williams, D. L. 2005. Analysis of tear uptake by the Schirmer tear test strip in the canine eye. *Veterinary Ophthalmology*, **8**(5): 325-330.
- Williams, D. L. 2010. Lack of effects on lymphocyte function from chronic topical ocular cyclosporine medication: a prospective study. *Veterinary Ophthalmology*, **13**(5): 315-320.
- Williams, D., Middleton, S., Fattahian, H. and Moridpour, R. 2012. Comparison of hyaluronic acid-containing topical eye drops with carbomer-based topical ocular gel as a tear replacement in canine keratoconjunctivitis sicca: A prospective study in twenty five dogs. *Veterinary Research Forum*, **3**(4):229.
- Yoon, H. Y., Min, B. S., Kim, S. Y., Lee, D. E. and Kim, J. H. 2016. Surgical management of parotid salivary duct rupture secondary to non-iatrogenic trauma in a dog. *Journal of Veterinary Medical Science*, **16**: 221.
- Zeev, M. S. B., Miller, D. D. and Latkany, R. 2014. Diagnosis of dry eye disease and emerging technologies. *Clinical Ophthalmology (Auckland, NZ)*, **8**: 581.



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<b>Title of M.V.Sc. Thesis</b>	<b>"Evaluation of cyclosporine and parotid duct transposition for management of KCS in dogs".</b>
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## Certificate-IV

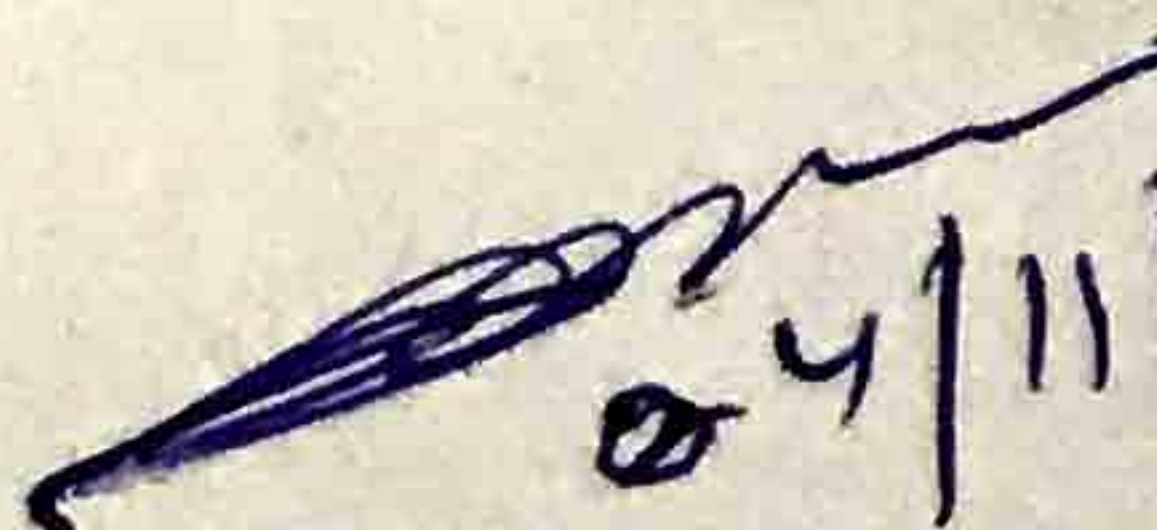
Certified that all the necessary corrections as suggested by the external examiner / evaluator and the advisory committee have been duly incorporated in the thesis entitled "Evaluation of cyclosporine and parotid duct transposition for management of KCS in dogs" submitted by Anmol Watal, Regd. No. J-17-MV-513.



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