CLINICO-BIOCHEMICAL AND ULTRASONOGRAPHIC EVALUATION OF RENAL FAILURE IN DOGS

KANARAN P. P.

Thesis submitted in partial fulfillment of the requirement for the degree of

Master of Veterinary Science

Faculty of Veterinary and Animal Sciences
Kerala Agricultural University, Thrissur

2009

Department of Clinical Veterinary Medicine
COLLEGE OF VETERINARY AND ANIMAL SCIENCES
MANNUTHY, THRISSUR-680651
KERALA, INDIA

DECLARATION

I hereby declare that the thesis entitled "CLINICO-BIOCHEMICAL AND ULTRASONOGRAPHIC EVALUATION OF RENAL FAILURE IN DOGS" is a bonafide record of research work done by me during the course of research and that the thesis has not previously formed the basis for the award to me of any degree, diploma, associate ship, fellowship or other similar title, of any other University or Society.

Mannuthy

KANARAN. P. P.

CERTIFICATE

Certified that the thesis entitled "CLINICO-BIOCHEMICAL AND ULTRASONOGRAPHIC EVALUATION OF RENAL FAILURE IN DOGS" is a record of research work done independently by Kanaran,P.P., under my guidance and supervision and that it has not previously formed the basis for the award of any degree, fellowship or associate ship to him.

Mannuthy

Dr.P.C.Alex
(Chairman, Advisory Committee)
Professor and ADR
Kerala Agricultural University

CERTIFICATE

We, the undersigned members of the Advisory Committee of Kanaran,P.P., a candidate for the degree of Master of Veterinary Science in Clinical Veterinary Medicine , agree that the thesis entitled "CLINICO-BIOCHEMICAL AND ULTRASONOGRAPHIC EVALUATION OF RENAL FAILURE IN DOGS" may be submitted by Kanaran,P.P., in partial fulfillment of the requirement for the degree.

Dr.P.C.Alex
(Chairman, Advisory Committee)
Professor and ADR
Kerala Agricultural University

Dr. K.M. Jayakumar
Associate Professor and Head
Department of
Clinical Veterinary Medicine
Biochemistry
College of Veterinary and
Animal Sciences, Mannuthy
(Member)

Dr. N.Divakaran Nair,
Professor
Centre of Excellence
In Pathology

College of Veterinary
and Animal Sciences,
Mannuthy (Member)

Dr.Usha Narayana Pillai
Associate Professor
Department of
Clinical Veterinary Medicine
College of Veterinary and
Animal Sciences, Mannuthy
(Member)

17/7
C N. Alaka Singe
External Examiner
Professor & COE
S.V. Vety. University
Tirupathi.

ACKNOWLEDGEMENTS

It is almost two years since I have returned to my Alma matter 23 years after graduation. During this period I have worked with many people whose contributions helped me to compile this thesis. It is a pleasure to convey my gratitude to them in my humble acknowledgement.

In the first place I would like to record my gratitude to Dr.P.C.Alex, chairman of my advisory committee, for his supervision, advice and guidance from the very early stage of this research and for the unflinching encouragement and support through out this work.

I gratefully acknowledge Dr.K.M.Jayakumar,Dr.Usha Narayana Pillai and Dr.N.Divakaran Nair, members of my advisory committee for their inspiring advice , valuable suggestions and encouragement throughout the study.

I wish to express my sincere thanks to Dr E. Nanu, Dean, College of Veterinary and Animal Sciences for the facilities provided.

I am gratefully acknowledging the contribution of my respected teachers Dr M. R. Saseendranath and Dr J. Saradamma.

I remember with thanks Dr Ajith Kumar, Dr Premni Elias, Dr Madhavan Unni and Dr Biju P Habeeb of the Department of Clinical Medicine for the help rendered.

My special thanks to Dr V R Ambily, my colleague who was always considerate, caring and affectionate.

I acknowledge the help rendered by my departmental colleagues Dr Unnikrishnan, Dr Ayub, Dr P Selva Kumar and Dr Girish Kumar, PG scholars Dr Elso John, Dr Dhanya V Pai, Dr Midhun, Dr Ganesan, Dr Pramod, Dr Rojan, my juniors Dr Ashwin, Dr Sindhu, Dr Raji and Dr Anju. all the other P G scholars and final year under graduates.

The help and co cooperation extended by the staff members of the department of clinical medicine is gratefully acknowledged.

I am indebted to the Department of Animal Husbandry for granting me deputation to undergo PG studies.

Finally to my family Anitha, Arun and Arjun whose love and support helped me to tide over the stress and strain of this some what delayed venture.

Kanaran

CONTENTS

LIST OF TABLES

LIST OF PLATES

LIST OF FIGURES

LIST OF PLATES

Introduction

1. INTRODUCTION

The kidney is a remarkable organ. It can adapt to the nephron loss from a wide range of insults such as hypoperfusion, nephrotoxins, diseases like systemic lupus erythematosus and severe hypertension and many others. The surviving nephrons compensate the damage by increasing their rate of excretion. In fact these adjustments are so subtle and noticed only when most of the nephrons are nonfunctional. Consequently diagnosis of kidney dysfunction is arrived so late mostly when the condition has progressed to renal failure.

Renal disease refers to any pathologic process occurring in kidneys. Left undiagnosed, renal disease often progresses to renal failure which occurs when kidneys lose their ability to function optimally. But if renal disease is diagnosed and properly treated, renal failure can be delayed or even avoided. Acute renal damage often results from ischaemic or toxic insults and usually affects the most metabolically active tubular portions of the nephron. In contrast chronic renal disease can be caused by diseases and disorders that affect any portion of the nephron, including its blood supply and surrounding interstitium.

Blood urea nitrogen and creatinine are the two most common parameters used to assess the renal function. The term azotaemia describes an elevation in one or both of these parameters due to changes in the glomerular filtration rate and does not indicate renal disease prior to failure. But when early renal disease is suspected the ability of the kidney to concentrate urine is to be evaluated and this perhaps is the most neglected procedure in veterinary medicine. Performed properly, urinalysis, specifically the measurement of urine specific gravity can be a measure of tubular function.

Results of recent studies suggested that in dogs and cats, as in humans, persistent proteinuria was associated with greater frequency of renal morbidity, renal mortality and mortality from all causes and the risk of these adverse outcomes increased as the magnitude of proteinuria increased (Lees et al., 2005). In dogs, Urine protein creatinine ratios (UPC) $\geq$ 0.5 are evidence of

adverse outcomes increased as the magnitude of proteinuria increased (Lees et al., 2005). In dogs, Urine protein creatinine ratios (UPC) $\geq$ 0.5 are evidence of persistent renal proteinuria, when they are found repeatedly in three or more specimens obtained two or more weeks apart and cannot be attributed to a pre renal or post renal cause. In dogs with renal failure having a UPC value $\geq$ 1.0 at initial evaluation is associated with increased risk of uremic morbidity and mortality. Urine protein creatinine ratios $\geq$ 2.0 usually is due to glomerular renal disease (Center, 1985).

A number of enzymes have been employed as markers of renal tubular dysfunction including the brush border enzymes alkaline phosphatase, γ Glutamyl transpeptidase and lysosomal enzyme N-acetyl-β-D-glucosaminidase which are excreted into the urine when released from the proximal tubular epithelium following tubular insult or injury.

Ultrasonography is an excellent method for evaluating the kidneys. Renal Ultrasonography provides a better means for evaluating general parenchymal architecture. It is particularly useful in differentiating solid from fluid lesions and in assessing the intrarenal distribution of such lesions. Renal ultrasonography is a complimentary procedure in the diagnostic evaluation of patients with renal disease.

Management strategy of acute renal failure includes removal of known causes of renal injury and supportive therapies directed to the life threatening consequences of acute uraemia. Animals with mild renal damage may regain adequate function within 3-5 days, but many of the moderate and severe cases die within 5-7 days. This underlines the importance of early diagnosis. A plausible method of treatment of moderate cases of acute renal failure is peritoneal dialysis which can be implemented in most veterinary institutions.

Treatment of chronic kidney disease includes specific therapy, prevention and treatment of complications of decreased kidney function,

management of comorbid conditions and therapy designed to slow loss of kidney function. Renal lesions in chronic kidney disease are irreversible and cannot be eliminated by therapy.

The incidence of renal failure has increased during the past few years and this might be due to the increased exposure to nephrotoxic substances which include a variety of therapeutic and other agents of day to day use such as food additives. Increasing incidence of leptospirosis is reported to be another important cause. Early diagnosis and timely treatment may help to delay the progression of the disease and increase the survival rate of the animals. Hence the present study was undertaken with the following objectives.

1. To study the occurrence of renal failure among dogs.

2. To study the ultrasonographic findings along with the clinicopathological observations.

3. To suggest suitable line of therapy.

Review of Literature

2. REVIEW OF LITERATURE

2.1 STRUCTURE AND FUNCTION

The basic unit of kidney is nephron. At one end of the nephron is the Bowman's capsule which is a double walled cup shaped structure containing a capillary bundle (the glomerulus) derived from an afferent arteriole. Just before leaving the Bowman's capsule the capillaries reform into an efferent arteriole which eventually supplies a capillary bed to the proximal convoluted tubules of the same nephron. The efferent arteriole is of a smaller caliber than the afferent, thus helping to maintain blood pressure within the glomerulus. (Drake, 1965)

Kelly (1967) reported that the renal blood flow was approximately 25% of the resting cardiac output. Reduced renal blood flow occurred after severe haemorrhage, during acute abdominal crises such as necrotizing pancreatitis and following dehydration associated with severe vomiting and diarrhea. This event caused reflex renal vasoconstriction and led to reduced blood flow to the nephron. This ischaemia could result in slight glomerular swelling and parenchymatous degenerative changes of varying severity in tubular epithelial cells.

The glomerular capillary tuft was an invagination into the dilated Bowman's capsule. In the glomerulus, plasma was filtered through the capillary endothelium and the capsular epithelium by the hydrostatic pressure of blood. Water and small molecular weight substances such as urea, uric acid and creatinine passed through the glomerular pores into the capsule and thence to the proximal convoluted tubules. Glomerulus is impermeable to large molecular weight substances such as proteins. Serum albumin is normally retained by the glomerulus although very small amounts may enter the filtrate and be resorbed in the tubules. Slightly smaller

molecules such as haemoglobin pass from the plasma into the glomerular filtrate (Forrester *et al.*, 1994)

The tubular system of nephron consists of the proximal convoluted tubules, the descending and ascending limbs of the loop of Henle, the distal convoluted tubules and the collecting ducts. In general terms the main function of the tubules were (a) resorption of essential metabolities (b) resorption of ions important for the maintenance of acid base balance (c) secretion of certain ions such as H+, K + and NH4 + and (d) reabsorption of water. (DiBartola, 2005)

2.2 RENAL FAILURE

The term renal failure refers to the clinical syndrome that occur when the kidneys are no longer able to maintain their regulatory, excretory and endocrine functions resulting in retention of nitrogenous solutes and derangements of fluid, electrolytes and acid base balance. Renal failure occurred when 75% or more of the nephron population was nonfunctional. (DiBartola, 2005)

2.2.1 Acute renal failure (A.R.F)

ARF occurs with disorders that cause either nephrosis or nephritis. Nephrosis was the most common cause in dogs and cats and usually occurred secondary to toxicosis and to a lesser extent to renal ischaemia (Forrester and Little, 1994).

Acute uremia is a clinical condition in which the kidneys suddenly fail to meet the excretory, metabolic and endocrine demands of the body. This abnormality was induced by rapid hemodynamic, filtration, tubular, interstitial or excretory injury to the kidneys or out-flow system or both which resulted in the accumulation of solutes (uremic toxins), metabolic dysfunctions and deregulation of fluid, electrolyte and acid base balance (Cowgill and Francey, 2005).

Azotaemia is defined as the increased concentration of nitrogenous compounds in the blood; usually urea and creatinine. Prerenal azotaemia was a consequence of reduced renal perfusion and postrenal azotaemia resulted from interference with excretion of urine from the body. Primary renal azotaemia was caused by parenchymal renal disease. (DiBartola, 2005)

Etiology

Infectious causes

Keenan *et al.* (1978) reported leptospirosis as the most clinically important cause of nephritis and ARF in dogs. The organism penetrated mucous membrane or abraded skin, multiplied in blood stream and then colonized renal tubular epithelial cells where pathologic damage ensued. Leptospires produced a toxin that directly affected capillary structure and function.

Renal vascular compromise resulting from thromboembolism of renal artery and vein, disseminated intravascular coagulation and renal infarction due to septic emboli from left sided bacterial endocarditis might cause acute renal failure. Infections like Rocky Mountain spotted fever, ehrlichiosis and bacterial endocarditis could cause renal pathology. The renal endarterial circulation rendered the kidneys vulnerable to damage by rickettsiae. They invaded and replicated in capillary endothelial cells causing a necrotizing vasculitis (Forrester and Little, 1994).

Birnbaum *et al.* (1998) observed that the most common clinical presentation of leptospirosis was acute renal failure and *Leptospira pomona* and *Leptospira grippotyphosa* were the important pathogens capable of causing severe renal and hepatic injury in dogs.

Non infectious causes

Meynard, (1975) reported nine cases of traumatic rupture of bladder in dogs out of which eight recovered after surgery and one dog developed acute uraemic nephritis and died.

Jayathangaraj *et al* (1993) reported a case of secondary acute renal failure in a dog which was treated with oxytetracycline @7 mg/Kg bodyweight for prostatitis.

Forrester and Brandt (1994) reported that radiographic contrast media (2.2 ml/kg of 75% diatrizoate meglumine/diatrizoate sodium) associated ARF was reported in a dog. Concurrent disorders of dehydration, diabetes mellitus and renal disease appeared to be a greater risk for this toxicosis. Excessive administration of inhalational anaesthesia was also a predisposing factor. Rodenticide intoxication could cause renal vaso-constriction and subsequent renal failure in dogs.

Many drugs like aminoglycosides, amphotericin B, cisplatin, oxytetracycline and thiacetarsamide caused ARF by nephrotoxicosis. Aminoglycosides (gentamicin) interfered with renal tubular reabsorption, causing tubular necrosis and decreased glomerular filtration rate (GFR) which led to reduced elimination of the drug which potentiated renal injury. Gentamicin toxicity could occur at the recommended dosage of 2.2 mg/kg TID or at higher dosages depending on individual variables such as age, hydration status, renal function and use of concurrent drugs. Oxytetracycline caused decreased urine concentrating ability and renal tubular damage. Thiacetarsamide interfered with renal tubular enzymes and transport system, resulting in tubular necrosis and renal failure. (Forrester *et al.*, 1994)

Non steroidal anti-inflammatory drugs (NSAIDS) interfere with kidneys normal ability to counteract systemic vasoconstriction resulting in renal ischaemic injury. Administration of Ibuprofen, naproxen, phenylbutazone and flunixin meglumine could cause renal injury. NSAIDs inhibited cyclooxygenase and interfered with the production of vasodilatory prostaglandins, (PGE 2 and PGI 2) which were responsible for the maintenance of renal perfusion and GFR in the phase of vasoconstriction in sensitive patients.Renal ischaemia, hypovolaemia, heat stroke etc resulted in ARF. Heat stroke caused systemic vasodilatation and resulted in the development of ARF due to decreased systemic vascular resistance. Other side effects of heat stroke were dehydration, rhabdomyolysis, myoglobinuria and disseminated intravascular coagulation. (Forrester and Little, 1994)

Acute intrinsic renal failure in a two years old male German Shepherd dog following a viper bite was reported by Puig.*et al.* 1995.

Kraje (2002) reported that cisplatin and Amphotericin B were nephrotoxic drugs. Cisplatin caused a dose dependent renal tubular necrosis. Most animals with normal renal function tolerated a dose of 60-70 mg/m2 when appropriate preventive measures were taken. Amphotericin B would get bound to sterols in renal tubular cells causing increased tubular permeability resulting in loss of chloride in urine. Increased excretion of chloride was sensed by macula densa of distal tubule, which through the tubulo glomerular feed back mechanism caused renal vasoconstriction. The end result was reduced renal blood flow and GFR and subsequent azotaemia.

Ethylene glycol got converted to metabolites glyoxalate and oxalate by hepatic alcohol dehydrogenase, which inhibited important cellular enzymes and interfered with cellular respiration and caused renal tubular necrosis. Tubular

deposition of calcium oxalate crystals might contribute to renal injury but was not essential for pathogenesis. (Cowgill and Francey, 2005)

Bruchim *et al.* (2006) opined that disseminated intravascular coagulation and acute renal failure were the risk factors for death in cases of heat stroke.

Jacobson (2006) observed that the prevalence of ARF due to canine babesiosis in hospitalized cases were 2.2% while 34% of the dogs with complicated babesiosis had elevated creatinine levels.

Fang *et al.* (2008) suggested that tar fruit juice produced acute renal injury, not only through the obstructive effect of calcium oxalate crystals, but also by inducing apoptosis of renal epithelial cells which might be caused by the levels of oxalate in the fruit.

Hutton *et al.* (2008) opined that only minimal evidence of the presence of intact *Borrelia burgdorferi* or any other bacterial organism was found in the renal tissue of dogs suspected having "lyme nephritis" characterized by persistent proteinuria and fatal renal failure.

Qari (2009) reported a case of severe rhabdomyolysis and acute renal failure secondary to use of simvastatin , an anticholesterolaemic drug, in a man with undiagnosed hypothyroidism

2.2.2 Chronic Renal Failure (CRF)

Leifer *et al* (1987) reported a case of proliferative glomerulonephritis in a 10 year old spayed female Labrador retriever dog associated with

Corynebacterium parvum immunotherapy in a dog and the disease was suspected to be of immune complex origin perhaps initiated by *C.parvum* treatment.

Glomerulonephritis and amyloidosis were the two primary glomerular diseases. Glomerulonephritis was caused by the deposition of Antigen-Antibody complexes as a result of diseases like pyometra, dirofilariasis, mastocytoma and systemic lupus erythematosus, in the glomeruli causing inflammation and tissue damage. Amyloidosis was caused by the deposition of the glycoprotein amyloid with β pleated conformation which might be associated with chronic suppurative diseases, necrotic diseases or neoplasia (Fleming *et al.* 1989)

Mikiciuk *et al.* (1989) opined that when a disease process caused loss of functional nephrons and the kidneys unable to compensate, the result was chronic renal failure. The authors observed that chronic tubular and interstitial renal disease resulted from many disease processes that produced interstitial fibrosis, tubular atrophy, focal mononuclear cell infiltration and glomerulosclerosis. Often the acute stage of inciting disease was subclinical. Chronic obstruction, chronic leptospirosis, Canine adenovirus I infection, pyelonephritis and glomerulonephritis eventually produced chronic interstitial disease.

Urine out flow obstruction resulted in hydronephrosis and if complete, both kidneys were affected resulting in renal failure. Bilateral hydroureter and hydronephrosis in a nine year old female German shepherd dog following a past surgical procedure (ovario hysterectomy) was reported by Gopegui et *al.* (1999).

Struvite renal stones were most common in dogs and could be caused by urinary tract infection, alkaluria, genetic factors or factors in diet (Mishina *et al.* 2000).

Pressler and Vaden (2003) suggested that 23% of protein losing nephropathies in dogs were due to amyloidosis which eventually led to renal failure. Two forms of systemic amyloidosis, reactive amyloidosis and immunoglobulin light chain associated amyloidosis have been shown to occur in dogs and cats.

Glomerulocystic kidney was diagnosed by Takahashi *et al.* (2005) in a 5 year old female shiba dog which died from chronic renal failure with convulsions, vomiting etc. Stones could cause severe blockage and local tissue irritation resulting in renal damage.

Cortadellas *et al.* (2006) found that systemic hypertension was prevalent in dogs with renal disease secondary to leishmaniasis, not only in the more severe stages but also in the early course of the illness before azotaemia became apparent.

Locke and Barber (2006) reported that dogs with renal haemangiosarcoma (HSA) have protracted disease progression, with improved one year survival rates and longer median survival time compared to dogs with splenic, cardiac, and retroperitoneal HSA.

Plevraki *et al.* (2006) quoting previous reports said that immune complex glomerulonephritis and tubulointerstitial nephritis have been incriminated as the main causes of asymptomatic proteinuria, nephritic syndrome and chronic renal failure seen in cases of canine leishmaniosis.

2.3 SIGNALMENT

2.3.1 Age

In juvenile onset renal disease of Doberman pinschers, affected dogs were below 2 years of age (Miles *et al.*, 1986).

Center *et al.* (1987) in a retrospective study of 10 years, evaluated the clinicopathological, renal immunofluoroscent and light microscopic features of glomerulonephritis in dogs and found that the cases could be segregated into membraneous, mesangioproliferative or membranoproliferative and no significant differences existed among groups with regard to age or duration of illness

Mikiciuk *et al.* (1989) listed a number of hereditary nephropathies in young dogs in an exhaustive review of chronic renal failure. The dogs affected were young and most of them were less than one year old with range from one month to 5 years.

Polzin (1990) opined that renal failure and urinary incontinence were the most prominent geriatric complications in dogs. The most characteristic lesion of renal aging in man and rats was glomerular sclerosis and such lesions were also observed in aged dogs.

Eubig *et al.* (2005) recorded acute renal failure in Dogs after the ingestion of grapes or raisins and the median age was 4.0 years (range 0.6–13.0 years).

Bryan *et al.* (2006) in a retrospective study on primary renal tumours in dogs reported that carcinomas, sarcomas and nephroblastomas were the prevailing primary tumours in dogs. Mean age of affected dogs was 8.1 years with a range of 1-17 years.

Chandler *et al.* (2007) reported juvenile nephropathy in 37 young boxer dogs below five years of age with chronic renal failure.

2.3.2 Sex

Vaden *et al.* (1997) concluded from a retrospective study of acute renal failure that intact male dogs were more likely to develop ARF.

Birnbaum *et al.* (1998) observed no sex predisposition in dogs naturally infected with leptospirosis.

Antony (2004) while reporting on urinary tract disorders in dogs found that 63% of affected dogs were males.

Eubig *et al.* (2005) reported that among dogs with acute renal failure after the ingestion of grapes or raisins 62.8% were males.

2.4 PATHOPHYSIOLOGY

Extrapolating from the model of rodents, Brenner *et al* (1982) suggested that there was an inherent tendency for progressive loss of renal function in all mammals. While renal injury initially led to beneficial adaptive changes in renal structure and function, eventually these adaptive changes became excessive or maladaptive, contributing directly to renal injury.

Bell *et al.* (1984) reported a progressive nephropathy in rats with spontaneous structural changes that occured with advancing age including thickening

of tubular and glomerular basement membrane, mesangial proliferation, epithelial foot process fusion and ultimately obliterative glomerulosclerosis. Associated functional changes included proteinuria and eventual decline of glomerular filtration rate. The severity increased with age and could be hastened by partial nephrectomy or modified by a variety of dietary manoeuvres.

Bourgoignie *et al.* (1987) in a study of female mongrel dogs which were examined for upto 39 months after 7/8 nephrectomy found that 2/10 dogs exhibited a pattern of progressive decline of GFR with proteinuria and glomerular lesions. Most of the animals developed structural renal lesions which were glomerular and interstitial in location. However only a minority of animals exhibited progressive renal disease.

Dogs and cats with a decreased renal function had an adaptive preglomerular vasodilation permitting transmission of elevated arterial pressure to the glomerular capillaries. Studies indicated that systemic hypertension was present in most dogs and cats with clinically diagnosed chronic renal failure. On the basis of studies in rats, people and diabetic dogs, angiotensin converting enzymes inhibitors appeared to be the agent of first choice for antihypertensive therapy in renal diseases (Brown, *et al.*, 1997)

Pathophysiological consequences of persistent proteinuria in dogs included decreased plasma oncotic pressure, hypercholesterolaemia, systemic hypertension, hyper coagulability, muscle wasting and weight loss (Grauer, 2005).

2.5 CLINICAL SIGNS

In acute renal disease the onset of signs would be abrupt and the signs included anorexia, depression, vomiting and thirst. The rectal temperature was often normal, but an arched back, stiff gait, pain in the lumbar region, and full pulse could

be encountered. In chronic cases, signs were progressively increasing thirst, polyuria, and loss of weight. In more advanced cases, anorexia, vomiting, halitosis and dyspepsia were observed. Uraemia with necrosis of tongue was a late sign. (Doxey, 1983).

Mikiciuk *et al.* (1989) said that regardless of the underlying cause, the presenting signs and laboratory findings in CRF were the same. The animal was usually polyuric and polydipsic and exhibited clinical signs of uraemia, such as weight loss, anorexia, vomiting and diarrhea. The animal might also be depressed and had an increased depth of respiration.

Historical and physical examination findings supportive of acute renal failure included an acute onset of vomiting, diarrhea, halitosis, oral ulceration, anorexia, tachypnoea, dehydration, depression, hypothermia and normal to large possibly painful kidneys. Patients with chronic renal failure often had long standing weight loss, polyuria, polydipsia, vomiting and diarrhea as well as small kidneys with irregular margins.(McCaw *et al.*,1989a)

Puig *et al.* (1995) reported the clinical signs following snake bite in a German shepherd dog as depression, hypersalivation, vomiting, tachypnoea, abdominal pain, spleenomegaly, oliguria with haematuria, and haemolysed serum.

Gopegui *et al.* (1999) reported a case of bilateral hydronephrosis and hydroureter in a German Shepherd dog and that at the time of initial presentation the dog was vomiting, moderately dehydrated, depressed, hypothermic and emaciated. Physical examination revealed pale mucous membranes and an abdominal mass located in the right sublumbar area.

Eubig *et al.* (2005) reported that after the Ingestion of Grapes or Raisins, dogs usually began vomiting within 24hours ; vomiting was followed by

development of anorexia, lethargy, and diarrhea. Serum creatinine and phosphorus concentrations increased soon after exposure, whereas BUN tended to increase 24 hours later,and serum calcium concentrations increased 48 to 72 hours after exposure. Vomiting was a consistent finding

Goldstein *et.al* (2006) suggested that leptospira sero group Pomona caused more severe renal disease and was associated with a worse outcome compared with disease caused by other serogroups. They found that Common clinical signs of leptospirosis included lethargy, anorexia, and vomiting

Nicolle *et al.* (2007) reported that azotemia and renal impairment increased with the severity of congestive heart failure and were frequent findings in dogs with cardiovascular diseases. They commented that deterioration of renal function could be a direct result of progression of the heart disease. They also reported that the patient was thin and had a rough coat, oral ulceration, lingual discolouration and necrosis, mucosal pallor, injected sclera and dehydration. The size of the kidneys was smaller than normal.

2.6 ULTRASONOGRAPHY

Cook *et al.* (1977) observed that appearance of renal ultrasonogram varied according to the region of the kidney scanned.

Renal cortex, medulla, pelvis, pelvic diverticuli, interlobar vessels, peripelvic fat and renal capsule could be differentiated on ultrasonography of normal canine kidney. (Konde *et al.*, 1984)

Walter *et al.* (1987) opined that abdominal radiography, excretory urography, nuclear scintiagraphy and ultrasonography were complimentary diagnostic modalities used to evaluate renal disease. Because of the cranial position of right kidney in dogs, it was often necessary to image the right kidney through the

eleventh to twelfth intercostals spaces. The renal arteries and veins were often identified at the renal hilus.

Barr *et al.* (1990) studied the ultrasonographic measurement of normal renal parameters and found that there was a statistically significant correlation between renal length and body weight and renal volume and body weight

Lamb (1990) in a review of abdominal ultrasonography in small animals described the indications, examination techniques and interpretation of abnormal findings. The normal kidney had a uniformly echogenic cortex clearly demarcated from the hypoechoic to anechoic medulla. Interlobar vessels and renal diverticula subdivided the renal medulla. Sinus contained an echogenic fat pad.

Voros *et al.* (1993) pointed out that false positive diagnoses can happen in the diagnosis of cystic calculi using ultrasonography when urinary sludge of organic components, gas or air bubbles,blood clots, or bladder tumors and polyps were present. False negative diagnosis could be made when the bladder did not contain fluid, calculi were too small or when ultrasonography was not performed systematically.

In dogs, left kidney is caudal to the greater curvature of the stomach, caudodorsal to the spleen, and lateral to the aorta and left adrenal gland. It is a retroperitoneal organ and is at the level of the L2 to L4 vertebrae. The right kidney is caudal to the right liver lobes. The cranial pole of the right kidney is in the renal fossa of the caudate liver lobe. It was lateral to the caudal venacava and right adrenal gland and was generally more cranial than the left kidney at the level of the L1 to L3 vertebrae. (Nyland, 1995).

Triolo and Miles (1995) suggested that the major clinical indications for renal ultrasonography were a palpable renal abnormality, laboratory evidence of

urinary tract disease like haematuria, proteinuria or azotaemia, nonvisualisation of kidneys in survey radiographs, cases involving debilitated patients or those with severely impaired renal function, cases in which contrast radiography was contraindicated or would be nondiagnostic as a result of poor kidney opacification, monitoring of treatment response, and cases in which assistance was required in percutaneous renal biopsy.

Birnbaum *et al.* (1998) reported bilateral nephromegaly,hyperechoic renal cortices and mild renal pelvis dilation as abnormal ultrasonographic findings in dogs naturally infected with leptospirosis.

Forrest *et al.* (1998) reported that on ultrasound examination of 20 cases with confirmed leptospirosis,three had a normal ultrasonogram and the remaining had renal sonographic abnormalities. These included renomegaly,pyelectasia,increased cortical echogenicity and a medullary band of increased echogenicity which they postulated as a specific sonographic sign of leptospirosis.

Ultrasonographic features of a female German Shepherd dog with acute renal failure following hydronephrosis and bilateral hydroureters as reported by Gopegui *et al.* (1999) were pelvic distension and irregular cortex of the left kidney, severe hydronephrosis of the right kidney, bilateral hydroureter and the presence of a 4 cm hypoechoic oval mass medial to the right kidney. The ultrasonographic appearance of the urinary bladder, liver and spleen was however unremarkable.

Mantis and Lamb (2000) opined that the medullary rim sign on ultrasonography of the canine kidney had no associated demonstrable renal dysfunction.

Reusch *et al.* (2000) reported that in dogs with severe azotaemia ultrasonography of the parathyroid glands could aid in the differentiation of acute and chronic renal failure in dogs.

Armbrust *et al.* (2001) described the basics of renal ultrasonography and suggested that the echogenicity of kidney cortex was to be compared with that of spleen on the left and the liver on the right. The echogenicity of the renal cortex should be less than that of the spleen and less than or equal to that of the liver. These comparisons should be made at a similar depth and gain compensation. The renal cortex is hyperechoic relative to the medulla. The renal sinus was the most hyperechoic.

Widmer *et al.* (2004) opined that many infiltrative processes of the renal parenchyma resulted in fibrosis and replacement of functional tissue and therefore they might be ultrasonographically similar. Because of the tremendous reserve capacity of the kidney,renal echogenicity could not be related to function. He also pointed out that kidneys with end stage disease were often diffusely hyperechoic and have poor corticomedullary delineation and an irregular shape. In addition many kidneys with end stage disease were small and have decreased cortical thickness and irregular margination with thick capsules.Ethylene glycol toxicosis caused marked renal cortical and to a lesser extent medullary hyperechogenicity.

According to Chandler *et al.* (2007) the ultrasonographic findings in 37boxer dogs with juvenile nephropathy included hyperechoic renal cortices, loss of corticomedullary junction definition, dilated pelves and irregularly shaped small kidneys.

Holloway and O'Brien (2007) reported that localized perirenal retroperitoneal free fluid might be a useful ultrasonographic feature to assist with the characterization of and determination of prognosis in patients with suspected renal

disease. Perirenal effusion was seen in patients with acute renal failure due to nephrotoxicity, leptospirosis, ureteral obstruction, renal lymphoma, ureteronephrolithiasis, prostatic urethral obstruction, interstitial nephritis and ureteritis. Additional sonographic findings suggestive of renal parenchymal disease were mild, moderate or severe pyelectasia, increased renal echogenicity, increased or decreased renal size and ureteral or renal calculi.

Mareschal *et al.*(2007) examined the relationship of aortic luminal diameter(Ao) and renal length.(K). They opined that based on 95% confidence intervals ,renal size should be considered reduced if the K/Ao ratio is <5.5 and increased when it is >9.1.

Ivancic and Mai (2008) performed a prospective cross sectional study to qualitatively and quantitatively compare the echogenicity of the renal cortex relative to the liver in healthy dogs . They suggested that the renal cortex could be slightly hyperechoic to adjacent liver.

Haers and Saunders (2009) suggested that contrast enhanced ultrasonography could potentially aid in the discrimination between primary and secondary malignant renal lesions and increased the ability to detect lesions compared with conventional ultrasonography. It also improved the detection of fluid filled cavities.

2.7 HAEMATOBIOCHEMICAL ANALYSIS

2.7.1 Haemogram

Keenan *et al.* (1978) reported that Beagles experimentally infected with *Leptospira interogans serovar bataviae,* showed severe or moderate disease characterized by mild anaemia and a marked increase in ESR and plasma fibrinogen.

Haematologic results of juvenile onset renal disease in Doberman pinschers revealed non regenerative anaemia and lymphopenia (Miles, 1986).

Mikiciuk *et al.* (1989) in a review opined that the CBC of a CRF patient would reveal normochromic normocytic anaemia.

Acute renal failure patients would reveal anemia or a normal haematocrit and leucocytosis (Forrester and Brandt, 1994).

Puig *et al.* (1995) observed leukocytosis with shift to left in a dog with acute renal failure following snake bite.

Gopegui *et al.* (1999) in a case of chronic renal failure due to bilateral hydroureter and hydronephrosis following an operation for ovario hysterectomy found low PCV, anaemia, and a reticulocyte production index of 0.6 which indicated non regenerative anaemia.

Takahashi *et al.* (2005) in a five year old female Shiba dog with glomerulocystic kidney which died from chronic renal failure found non regenerative anaemia.

Kessler (2008) reported a case of secondary polycythaemia associated with high plasma erythropoietin concentration in a dog with necrotizing pyelonephritis. It was surgically removed and after surgery the haematological parameters and erythropoietin values returned to normal suggesting that pyelonephritis was the cause of polycythaemia.

2.7.2 Leucogram

Keenan *et al.* (1978) reported that Beagles experimentally infected with *Leptospira interogans serovar bataviae,* showed severe or moderate disease characterized by severe leukocytosis.

Miles (1986) opined that haematologic results of juvenile onset renal disease in Doberman pinschers revealed lymphopaenia.

Mikiciuk *et al.* (1989) in a review opined that the differential leucocyte picture of a CRF patient would reveal neutrophilia and lymphopaenia.

2.7.3 Platelet count

Keenan *et al.* (1978) reported thrombocytopaenia in Beagles experimentally infected with *Leptospira interogans serovar bataviae.*

Puig.*et al.* (1995) opined that the haematological findings associated with acute renal failure following snake bite included thrombocytopenia resulting in prolonged coagulation time.

2.7.4 Total protein, Albumin, Globulin, AG ratio

Goldstein *et al.* (2006) found that in dogs affected by *Leptospira pomona* , 35% had hypoalbuminaemia and 31% had hyperglobulinaemia.

2.7.5 BUN and Creatinine

Plasma creatinine was more efficient than plasma urea concentration for the diagnosis of CRF.(Biewenga *et al*,1981).

Mikiciuk *et al.* (1989) opined that if 75% of nephron mass was lost, azotaemia with isosthenuria would be present. Serum concentration of sodium and chloride were usually normal unless terminal oliguria was present. Metabolic acidosis with respiratory compensation was always present in these animals.

Gleadhill (1994) reported that dogs with renal insufficiency had higher creatinine values than normal dogs. The relative efficiency of creatinine and fractional excretion of phosphate as screening tests for early renal disease were

compared and found that for all decision levels, creatinine was superior to fractional excretion of phosphate.

Creatinine was increased in both ARF and CRF (Reusch *et al.*, 2000).

Braun *et al.* (2003) opined that plasma creatinine was more efficient than plasma urea concentration for the diagnosis of CRF. In dogs with spontaneous or surgically induced CRF, the correlation between plasma concentration of urea and creatinine were reported to be high or low but correlated well with concentration of plasma cystatin C. Plasma creatinine was increased in both acute and chronic renal failure.

Secondary renal diseases causing increased plasma creatinine include Babesiosis, Leishmaniasis, Leptospirosis, Borreliosis, Trypanosomiasis, Heart worm disease, encephalitozoonoses, malignant histiocytosis, pyometra, experimental intestinal obstruction, gastric dilatation and torsion, diabetes mellitus, hypercalcaemia caused by hyperparathyroidism or lymphoma, congenital or familial renal diseases like hereditary nephritis, renal dysplasia, Alport syndrome, glomerulosclerosis, familial nephropathy and glomerular vasculopathy and Fanconi syndrome (Braun *et al.*, 2003).

Braun *et al.* (2003) in an extensive review observed that creatinine was the analytic most frequently measured in human and veterinary clinical laboratories as an indirect measure of glomerular filtration rate (GFR). A moderate decrease in plasma creatinine was reported in 80% of dogs with portosystemic shunts or dogs with a surgically placed portocaval shunt. It was also noted in early babesiosis.

Medaille *et al.* (2004) evaluated the relationship between serum/plasma urea and serum/plasma creatinine and found that in 27.55% of the

cases, urea concentration was increased while creatinine was normal. In 1.6% of cases creatinine concentration showed higher values while urea was normal. They opined that this discrepancy could be due to the non renal factors and variation in muscle mass of the animals.

Takahashi *et al.* (2005) in a five year old female shiba dog with glomerulocystic kidney which died from chronic renal failure found non regenerative anaemia, azotaemia and high serum creatinine.

Bryan *et al.* (2006) in a retrospective study on primary renal tumours in dogs reported that carcinomas, sarcomas and nephroblastomas were the prevailing primary tumours in dogs. Abnormalities on serum chemistry values were minor and nonspecific. High BUN in 22 % of cases and high creatinine in 20 % of cases were reported.

Goldstein *et al.* (2006) found that 93% of dogs affected by *Leptospira pomona* had increased BUN and creatinine.

Chandler *et al.* (2007) reported azotaemia as the important clinicopathological finding in 37 boxer dogs diagnosed as having juvenile nephropathy.

2.7.6 Serum electrolytes

When experimentally infected with *Leptospira interogans serovar bataviae,* hyponatraemia, hypochloraemia, hypokalaemia, hyperphosphataemia and mild hypocalcaemia could be observed in beagle dogs (Keenan *et al.*, 1978)

Patients with chronic renal failure might have laboratory findings that revealed normal to decreased potassium, mild metabolic acidosis, a history of chronic azotemia and inactive urinary sediment.(Mikiciuk *et al.*,1989)

Hyperphosphataemia and hyperkalaemia are the hallmarks of acute renal failure (Forrester and Brandt, 1994).

Deguchi and Akuzawa (1997) reported that renal clearance of creatinine and urea was significantly lower and that of sodium and potassium were significantly higher in cats with chronic renal failure. The glomerular filtration of creatinine and urea and the urinary excretion of these four substances were significantly higher in cats with chronic renal failure. The tubular reabsorption rates of sodium and potassium were significantly lower in cats with chronic renal failure compared to those in normal cats, but there was no significant difference in urea and creatinine.

Rubin and LeClerc (2001) opined that renal failure produced hyperkalaemia only when the glomerular filtration rate was severely compromised producing either an oliguric or anuric state. Hyperkalaemia resulted from a combination of reduced distal tubular flow rates and reduced potassium excretion in the cortical collecting ducts.

2.7.7 Urinalysis

Qualitative

Grauer (1985) observed that proteinuria without evidence of urinary tract inflammation was the hallmark of glomerular disease.

Urinalysis typically revealed an inappropriate urine concentration with specific gravity less than 1.030 in dogs and might show evidence of infection (active sediment) tubular injury (casts, proteinuria or glucosuria) and glomerular injury (proteinuria). Additional diagnostic tests were indicated including urine

culture, imaging, measuring titres for infectious diseases and renal biopsy (McCaw *et al.*, 1989).

Albasan *et al.* (2003) observed that urine specific gravity was not affected by storage.

Gary *et al.* (2004) observed that exercise did not change the microalbuminuria status of dogs. Positive dogs were positive before and after exercise without any quantitative change and negative dogs were negative throughout

Urinalysis was an essential part of the diagnostic evaluation for all urinary and many metabolic diseases. Its assessment included evaluation of physical characteristics, biochemical parameters and microscopic sediment evaluation. The authors detailed the importance of specific gravity in renal disease. Hyposthenuria is defined as a USG <1.008 and for this the distal convoluted tubule must be intact. Patients with renal failure cannot dilute urine below 1.008. Isosthenuria is defined as a USG between 1.008 to 1.012 and reflects that the osmolality of urine is equal to that of plasma. It was be suggestive of primary renal failure (Reine and Langston, 2005).

Kuwahara *et al.* (2006) opined that higher urine protein/creatinine ratio was most likely to be associated with mortality in cats with chronic renal failure.

Chandler *et al.* (2007) reported azotaemia, isosthenuria and proteinuria as the important clinicopathological findings in 37 boxer dogs diagnosed as having juvenile nephropathy.

2.7.8 Urinary enzymes

***Urinary* N- acetyl-β-D-glucosaminidase (NAG)**

N- acetyl-β-D-glucosaminidase (NAG) is a lysosomal enzyme found predominantly in the proximal renal tubular cells. A high level of NAG urinary excretion with marked isoenzyme B excretion were commonly considered as an indicator of aminoglycoside nephrotoxicity(Ali-Miraftab *et al.*, 1988).

Reusch *et al.* (1991) reported the mean urinary NAG index as 1.6U/g of creatinine. Its activity remained high during active disease or a sustained toxic insult but fall to normal levels on recovery or removal of the toxin. Urinary NAG activity can be used in conjunction with other tests to assess disease activity and prognosis.

The mean urinary NAG index of healthy dogs as reported by Uechi *et al.* (1994) was 5.7 ± 3.4 U/g of creatinine.

Sato *et al.* (2002) reported that the mean urinary NAG index in healthy dogs was 3.2 ± 2.4 U/g of creatinine. But in dogs with chronic renal failure the range of values were 15.7-136.8U/g. Dogs with chronic renal failure showed an increase of NAG index before elevation of BUN and serum creatinine concentration. There were no significant correlation between BUN, serum creatinine and urinary NAG index in cases of chronic renal disease. Dogs with diabetes mellitus showed higher urinary NAG index. Dogs that had pyometra and exhibited renal insufficiency after ovariohysterectomy showed high values of NAG index before ovariohysterectomy.

Ebisawa *et al.*(2006) observed in a model of reduced kidney mass that urinary NAG levels appeared in the normal range after reduction in kidney mass as

long as the remaining nephrones functioned in a compensatory fashion.But a reduction in the number of nephrones resulted in a decline in urinary NAG levels.

Brunker *et al.*(2009) studied the urinary NAG index in healthy dogs and found it to be 1.10 ± 0.97 U/g.

Urinary GGT

Ward (1976) found that urinary Gama GT was a sensitive indicator of renal cellular injury provided that there was adequate urine flow and that the renal insult had not been too severe.

Urinary Gama Glutamyl transpeptidase enzyme from tubular cells was released into the urine when there was tubular necrosis, several days before a change in creatinine clearance or azotaemia (Greco, 1985).

Heiene *et al.* (1991) opined that measurement of urinary GGT could not be used to distinguish between ARF and CRF. The seventy of the histopathological lesions were also not to be assessed by these enzyme levels in ARF and CRF.

Rivers *et al.*(1996) analysed the potential diagnostic utility of urine GGT to creatinine ratio in an experimental model of canine aminoglycoside induced nephrotoxicity. A therapeutic dosage of gentamicin resulted in a two fold increase in the mean urine GGT to creatinine ratio, but not associated with clinically significant nephrotoxicity. In dogs given a nephrotoxic dosage, increase of mean GGT to creatinine values showed three times the base line values and it preceded clinically significant abnormalities in serum creatinine, urine specific gravity and UPC.

Mrudula *et al.* (2005) reported that there was significant elevation of urinary GGT in nephritis cases and most of them were chronic interstitial nephritis.

Brunker *et al.*(2009) studied the urine GGT values of healthy dogs and found it to be 13.49 ± 7.03U/g .

Urinary ALP

Heiene *et al.* (1991) reported that urinary alkaline phosphatase could be used as an indicator of acute renal damage in dogs. But no clear correlations could be found between urinary enzyme levels and the extent of morphological damage.

Mrudula *et al.* (2005) found that there were significant elevations of urinary alkaline phosphatase in canine nephritis cases.

2.8 CLINICAL MANAGEMENT/TREATMENT

Center *et al.* (1987) opined that treatment with glucocorticoids was inappropriate for glomerulonephritis in the dog.

Kirby (1989) opined that body weight, PCV, plasma protein levels and CVP measurements were to be monitored as more objective measures of hydration status.

Dietary protein restriction was employed in dogs and cats with renal failure for two distinct reasons. First in animals with severe renal failure, it was employed to reduce the generation of uremic toxins (Polzin (1990). In dogs with early renal failure that do not exhibit clinical signs of anaemia, dietary protein

restriction was advocated as a means to slow the progression from early to late renal failure.

Kidney international in its editorial review (1996) opined that the corner stones in management of rhabdomyolysis and myohaemoglobinuric acute renal failure were correction of hypovolaemia, enhancement of the clearance of heme proteins from the circulation and kidney and mitigation of the direct adverse consequences of heme proteins on the proximal tubular epithelium.

Brown *et al.* (1997) found that prolonged administration of angiotension converting enzyme inhibitors (Lisinopril) lowered intra glomerular pressure in uninephrectomized diabetic Beagles but the calcium channel antagonist TA 3090 (a derivative of diltiazem) did not.The authors also opined that moderate dietary protein restriction was not a highly effective means of slowing the rate of progression of chronic renal failure in dogs. But dietary supplementation with n-3,but not n-6, fatty acids showed most promising renoprotective effect in studies on dogs.Several growth factors had been implicated in glomerulosclerosis or had been shown to have direct effects on renal haemodynamics. These included retinoids, platelet derived growth factor, epidermal growth factors and transforming growth factor B, insulin like growth factor, growth hormone and thyroid hormone.

Treatment for acute renal failure following bilateral hydroureter and hydronephrosis in a nine year old German Shepherd dog was attempted with crystalloid intravenous fluids (40 ml/kg of ringers lactate solution over 6 hours for rehydration followed by 10 ml/kg/day with 5% glucose to improve diuresis. Frusemide 2.2 mg/kg every 8 hours, dopamine 2 mg/kg/minute, cimetidine 10 mg/kg every 8 hours, and ampicillin 20 mg/kg every 8 hours. But there was no clinical improvement or reduction in azotaemia after 48 hours (Gopegui *et al.* 1999).

Grauer *et al.* (2000) suggested that enalapril treatment was beneficial in dogs with naturally occurring idiopathic glomerulonephritis.

Mishina *et al.*(2000) reported that they could dissolve struvite nophroliths in two dogs with an aminoacid preparation containing methionine and lysine designed for use in renal failure patients

Toutain *et al.* (2000) found that in dogs with subclinical renal failure the free plasma enalapril concentration required to produce 50% of total inhibition of the converting enzyme was increased by 2.5 fold .

Kraje (2002) suggested that treatment of acute renal failure involved minimizing further renal damage by stopping nephrotoxic drugs or initiating specific therapy, if underlying disease was present. Correcting hypovolaemia, replacing ongoing fluid losses and maintaining blood pressure could improve the situation.. Assess urine production to determine whether a patient was anuric (minimal to absent urine production), oliguric (<1 ml/kg/hr after rehydration) or non oliguric (>1 ml/kg/hr). Also any complications that have resulted from acute renal failure had to be treated.

Langston (2003) proposed that peritoneal dialysis,haemodialysis and renal transplants could be considered as advanced renal therapeutic options when the standard therapies failed to yield the expected results.

Uechi *et al.*(2003) suggested that torasemide , a new loop diuretic could be effectively used for inducing dieresis in dogs and cats with lower dose and prolonged effect than frusemide.

The efficacy and safety of recombinant canine erythropoietin (rcEPO) therapy was evaluated by Randolph *et al.* (2004) in dogs with anemia of chronic renal failure and recombinant human erythropoietin (rhEPO)-induced red

cellaplasia. Recombinant rcEPO stimulated erythrocyte production in dogs with nonregenerative anemia secondary to chronic renal failure without causing the profound erythroid hypoplasia that can occur in rhEPO-treated dogs. They also observed that rcEPO was not as effective in restoring erythrocyte production in dogs that had previously developed rhEPO-induced red cell aplasia.

Polzin *et al.* (2005) opined that management goals of ARF treatment were to (1) correct fluid, electrolyte and acid base disturbances, 2, initiate diuresis, (3) manage systemic complications and 4. establish a prognosis for recovery. Intravenous fluid therapy remained the primary mode of treating ARF to correct fluid, electrolyte and acid base disorders, improve renal perfusion, initiate a diuresis and to hasten elimination of nephrotoxicants. Volume deficits should be replaced rapidly over the first four to six hours of therapy.

Plevraki *et al.* (2006) observed that Allopurinol not only lowered proteinuria in dogs but also prevented the deterioration of GFR and improved the tubulointerstitial, but not the glomerular lesions.Further, it resolved the azotemia in 5 of the 8 dogs admitted with second stage chronic renal failure . Consequently,treatment with allopurinol was advised in Canine Leishmaniasis cases with asymptomatic proteinuria or 1st–2nd stage chronic renal failure.

Dorval and Boysen (2007) reported that although complications were common, peritoneal dialysis was an effective renal replacement therapy for acute renal failure in cats. They found that peritoneal dialysis succeeded in allowing renal recovery in 5/6 cats treated. The complications noticed were subcutaneous oedema, hyperglycaemia, dialysate retention and hypoalbuminaemia.

Mathews and Monteith (2007) observed that renal recovery in dogs with acute renal failure secondary to leptospirosis was improved with the administration of diltiazem in addition to standard therapy.

Pomianowski *et al.* (2008) reported that peritoneal dialysis was an effective option in the case of acute renal failure.However it was insufficient when renal azotaemia was accompanied by other disease syndromes related to oxygen deficiency in tissues and haematological changes.

2.9 PROGNOSIS

Miles *et al.* (1986) opined that prognosis for animals affected with juvenile onset renal disease was unfavourable. Early diagnosis along with implementation of symptomatic and supportive medical therapy would slow the progression of clinical signs.

Gopegui *et al.* (1999) opined that the prognosis for acute renal failure following hydronephrosis was very poor.

Kraje (2002) observed that patients with non oliguric acute renal failure had a better prognosis than those with anuric or oliguric acute renal failure. Patients with acute renal failure due to infectious diseases had a better prognosis than those with toxic or ischaemic acute renal failure. Patients with toxin induced acute renal failure might have a better prognosis than those with ischaemia induced acute renal failure because tubular basement membranes might be more likely to remain intact with toxin induced damage. A poor prognosis was more likely if pre existing disease (eg. Cardiac or renal disease, neoplasia, pancreatitis) was present, a high number of complications occurred, several organ systems were involved, azotaemia was severe or there was long interval between diagnosis and treatment. Prognosis also worsened with increasing age.

2.10 PREVENTION

Humes (1984) observed that calcium competed with gentamicin for renal tabular binding sites and dietary calcium supplementation protected rats from aminoglycoside nephrotoxicosis

Brown (1985) stated that amino glycosides should be used only for short periods and the mean of treatment in Gentamicin associated ARF was 6.8 days with a range of 3-11 days.

Neer, (1988) opined that fluroquinolone antimicrobials often could be used instead of aminoglycosides to treat gram negative infection in nephrotoxic patients.

Grauer (1992) observed that feeding dogs a high protein diet for 21 days before treatment with gentamicin prevented a severe decline in glomerular filtration rate and lessened the severity of renal tubular necrosis..

Oglive (1993) opined that the best way to prevent cisplatin induced nephrotoxicosis in dogs was to follow a four hour saline loading protocol.

Forrester *et al.* (1994) opined that every effort should be made to prevent ARF because patients surviving ARF often sustain permanent renal dysfunction despite intensive care and aggressive treatment.

Materials and Methods

3. MATERIALS AND METHODS

The study was conducted in the department of Clinical Veterinary Medicine, College of Veterinary and Animal Sciences, Mannuthy. The duration of study was four semesters during the academic year 2007-08 to 2008-09.

Canine patients brought to the University Veterinary Hospital, Kokkalai and Veterinary College Hospital, Mannuthy conforming to the selection criteria were included in the study.

3.1 SELECTION OF CASES

Dogs showing clinical signs suggestive of renal failure, *viz* persistent vomiting, oliguria/ anuria , oral ulcers, diarrhea, polyuria, dehydration, lethargy, inappetence etc were subjected to serum creatinine estimation and animals having serum creatinine more than normal levels were selected for the study.

3.2 OUTLINE OF STUDY

Clinical samples were collected from healthy animals brought to the hospital and analysed for determining the normal values prevailing in the population.

3.2.1 History and clinical examination

Detailed history was collected and clinical examination was carried out as per proforma (Annexure-1).

3.2.2 Haemato-biochemical examination

Collection of clinical materials

Relevant clinical materials were collected at the time of admission. Five ml of whole blood was collected from saphenous or cephalic vein of the affected dog in dry glass vials containing EDTA at the rate of 1-2 mg per ml as anticoagulant (Benjamin, 1985). Blood samples were collected on the 7^{th} day of admission also.

About 10 ml of blood was collected in another vial on the day of admission and on 7^{th} day to separate serum for biochemical examination. Sera thus collected were used for immediate examination and part of it was stored at -20^0c for further examination.

Urine samples were collected by catheterization or cystocentesis on the first day as well as 7^{th} day into sterile screw capped vials and used for immediate analysis and also stored at -20^0c for further examination.

Haematology

Haemoglobin, Volume of packed red cells, Total leucocyte count, Differential leucocyte count and Platelet count were estimated on the day of admission and on the 7^{th} day as per the methods described by schalm *et al.* (1975).

Biochemical Examination

Blood urea nitrogen, Serum creatinine, Serum total protein, Serum globulin, A:G ratio and Serum GGT were estimated on first and after seven days using a semiautomatic analyzer; Secomam Basic as per the manufacturers instructions and using standard kits.

Urea was estimated by diacetyl monoxime method using standard kits from Agappe diagnostics pvt ltd, Ernakulam. (Marsh *et.al.*, 1965). Blood urea nitrogen was estimated dividing the urea concentration by 2.14.

Creatinine concentration was estimated using Jaffe's alkaline picrate method with standard kits supplied by Agappe diagnostics pvt ltd, Ernakulam (Slot, 1965).

Serum protein was estimated by direct biuret method using standard kits supplied by Agappe diagnostics pvt ltd, Ernakulam. (Gornall *et al.*, 1949)

Serum albumin was estimated using bromcresol green methodology with standard kits supplied by Agappe diagnostics pvt ltd, Ernakulam (Doumas, 1971).

Serum γGT was estimated using the method prescribed by Tietz (1986) with the standard kits supplied by Agappe diagnostics pvt ltd, Ernakulam.

Serum potassium was estimated by emission flame photometry using the machine systronics 128 as described by Oser (1971) on 1st and 7th days.

Urinalysis

Estimation of urine specific gravity and detection of protein in urine was done using uristik reagent strips manufactured by Dirui industrial company ltd, China on first and seventh day.

Estimation of protein and creatinine in urine and protein creatinine ratio were done using Secomam Basic semiautomatic analyzer as per manufacturers instruction on first and on seventh days using biuret and modified Jaffe's method respectively

The urinary alkaline phosphatase (ALP) was measured using Ecoline alkaline phosphatase kits supplied by Merck specialities pvt ltd ,Mumbai and was expressed in comparison with millimoles of creatinine in urine.

Urinary γ Glutamyl transpeptidase (γGT) was measured using Ecoline γGT kits supplied by Merck specialities pvt ltd , Mumbai and was expressed in comparison with m mols of creatinine in urine.

Urinary NAG

Colorimetric determination of N –Acetyl-β-Glucosaminidase in urine was done as per Gressner and Roebruck(1982) using the standard kits supplied by FAR srf,Verona,Italy. Two ml each of urine samples were centrifuged at 3000 rpm in microcentrifuge for five minutes and the supernatant was used for estimation of NAG. Manual assay was done using UV spectrophotometer Genesys and the wavelength selected was 405 nm. Absorbences of sample (AS), Blank sample (ABS) and Blank reagent (ABR) were measured and the NAG activity in U/L was calculated using the formula, activity in U/L= (AS-ABS-ABR) X 144. The values were expressed in comparison with grams of creatinine in urine.

Examination of Urine sediment

The urine samples were mixed well, poured into two ml microcentrifuge tubes and centrifuged at 3000 rpm for 5 minutes. The supernatant was discarded and the sediment resuspended, transferred to a slide and examined.

Culture and Sensitivity.

Culture and sensitivity tests of urine samples were done wherever indicated using the method described by Cowan and Ling(1981) and Cruickshank *et al.*(1975).

3.2.3 Ultrasound Scanning.

Equipment

Selected dogs were subjected to ultrasound scanning using mindray DC 6 Vet Ultrasound machine with 2.5,3.0, 5.0 and 7.5 Mhz transducer.

Ultrasound Scanning Procedure

Animal was placed in dorsal recumbency such that cranial portion of the image was oriented to the viewers left on sagital scan and right side of the animal to viewers left on transverse scan. Abdominal ultrasonographic examanation was performed with the animal in the dorsal or lateral recumbancy .

Preparation of the site required clipping the hair over the entire abdomen, including midway up the body wall over the right and left caudal intercostal spaces. Acoustic coupling gel was applied to the skin. Liberal amounts of acoustic coupling gel provided sufficient contact for the best image possible.

A sector transducer, which provided a smaller contact zone was preferred for imaging through intercostal space.

Depending on the size of the dog the highest frequency transducer was used which allowed adequate depth penetration. For medium to large breeds of dogs a 3.5 – 7.5 MHz transducer was used. Firm pressure on the transducer was applied to gain maximum contact and displace overlying bowel gas.

The ultrasonograms were reviewed for alterations in the echogenecity of renal parenchyma and renal size. The parenchymal lesions were classified into focal and diffused. The echogenecity of renal parenchyma was

described as normoechoic, hypoechoic, hyperechoic or mixed echogenecity. The image was recorded on electro magnetic tape and later photographed.

3.2.4 Treatment:

Treatment was given according to the clinical condition of the animal. Fluids, Antibiotics, Diuretics and Antemetics were given wherever indicated. Six animals which did not respond to routine treatment were subjected to peritoneal dialysis.

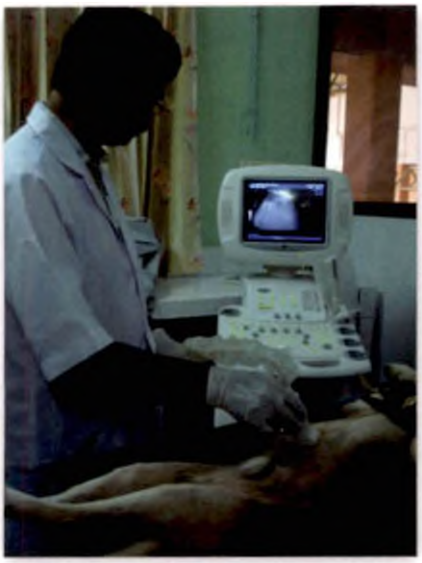
3.2.5 Postmortem examination and histopathology:

Post mortem examination was conducted on animals which died during treatment period and gross lesions were recorded. Samples from kidneys and other organs if necessary were taken for histopathology. The tissues were fixed in normal saline and were processed by routine paraffin embedding techniques as described by Sheehan and Hrapchak (1980). The sections were stained with Haematoxylin and Eosin as per techniques followed by Bancroft and Cook(1984) for evaluation of histological changes.

3.2.6 Statistical analysis

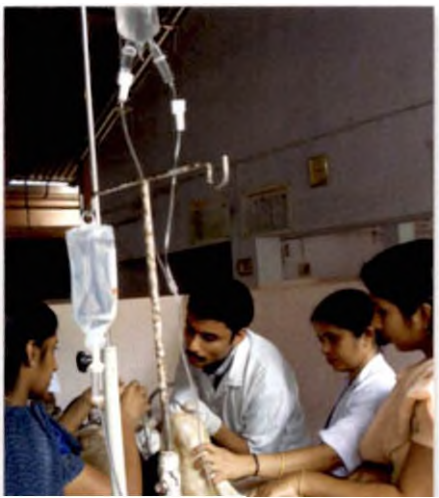
Data were analysed wherever indicated as per Snedecor and Cochran (1994).

Plate.1: Procedures



A:Ultrasonography

B:Peritoneal Dialysis - Catheter



Results

4. RESULTS

Dogs presented to the University Veterinary Hospital, Kokkalai and Veterinary College Hospital, Mannuthy that exhibited clinical signs suggestive of renal diseases and on biochemical examination having more than normal levels of serum creatinine were subjected to detailed clinical examination as per proforma, ultrasonographic evaluation, haematobiochemical analysis of serum and urinalysis. Urine of a few selected animals were subjected to estimation of renal tubular lysosomal enzyme N-Acetyl-β-D-Glucosaminidase and urinary brush border enzymes, γ- Glutamyl transpeptidase and Alkaline phosphatase. These values were compared with the values obtained from clinically normal animals.

A total of 23 cases were selected for the study. Out of the 23 cases, 15(65 %) were males and the rest were females. (Fig: 1).

The breeds represented in this study were eight German shepherd dogs(35%), seven nondescripts (30%), two Labradors(8%), and one each of Doberman, Neapolitan mastiff, Spitz, Dalmatian, Weimaraner and Rottweiler (4.5% each) (Fig:2).

Age of affected animals ranged from four months to 13 years. Dogs in the age group of 4-8 years were the most susceptible to renal failure. (Fig: 3).

Regarding vaccination status, 22/23 (96%) of the dogs were vaccinated against rabies and 15/23 (65%) were vaccinated with multicomponent vaccines which protected against canine distemper, canine parvovirus, leptospirosis and canine adenovirus. (Fig: 4)

Clinical signs observed indicated that all the dogs were suffering from lethargy and anorexia. Other clinical signs included vomiting (96%), melena (78%),

Fig.1: Signalment-Sex

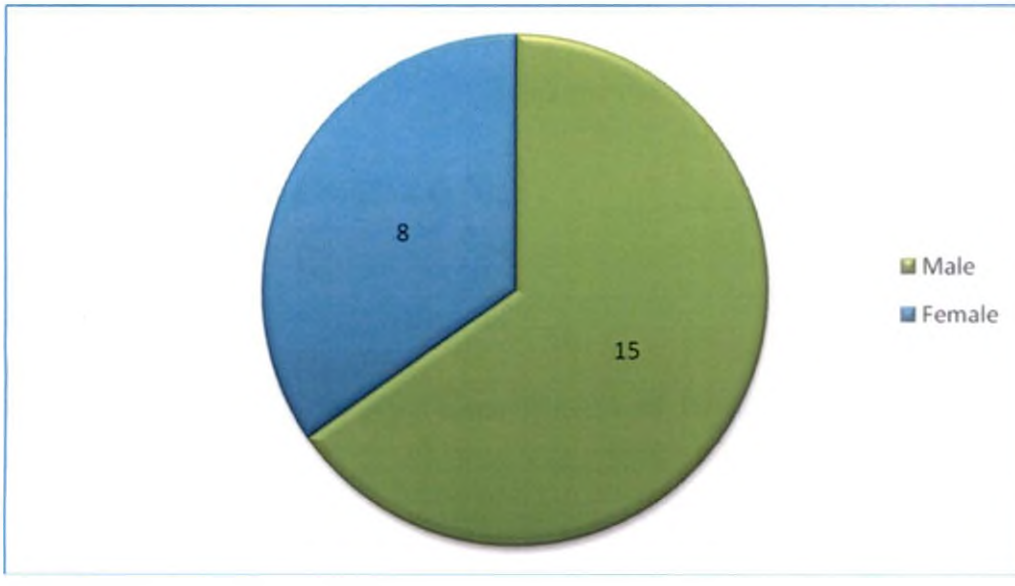


Fig.2: Signalment-Breed

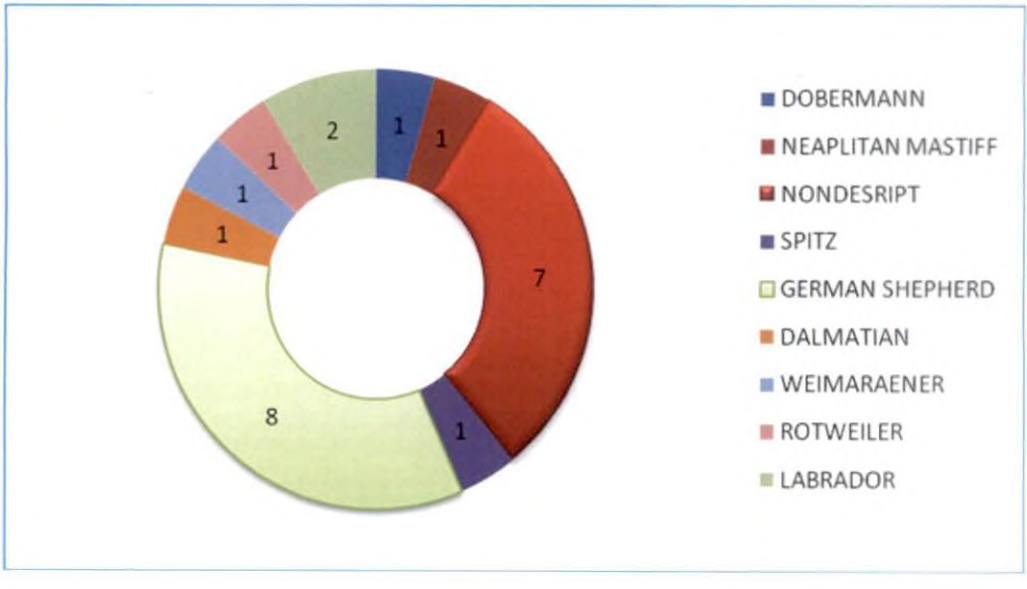


Fig.3: Signalment: Age

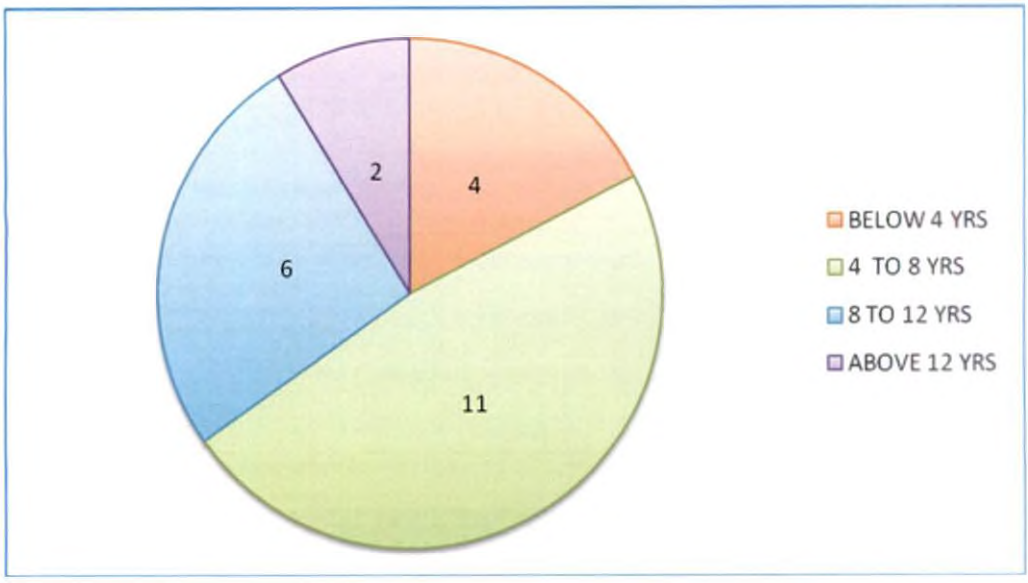


Fig.4: Vaccination status

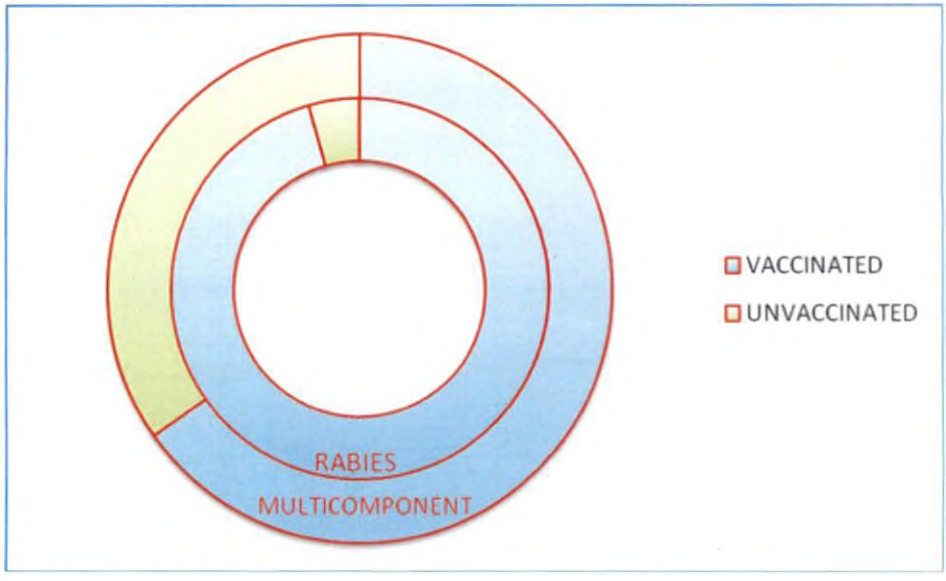


Fig.5: Clinical signs

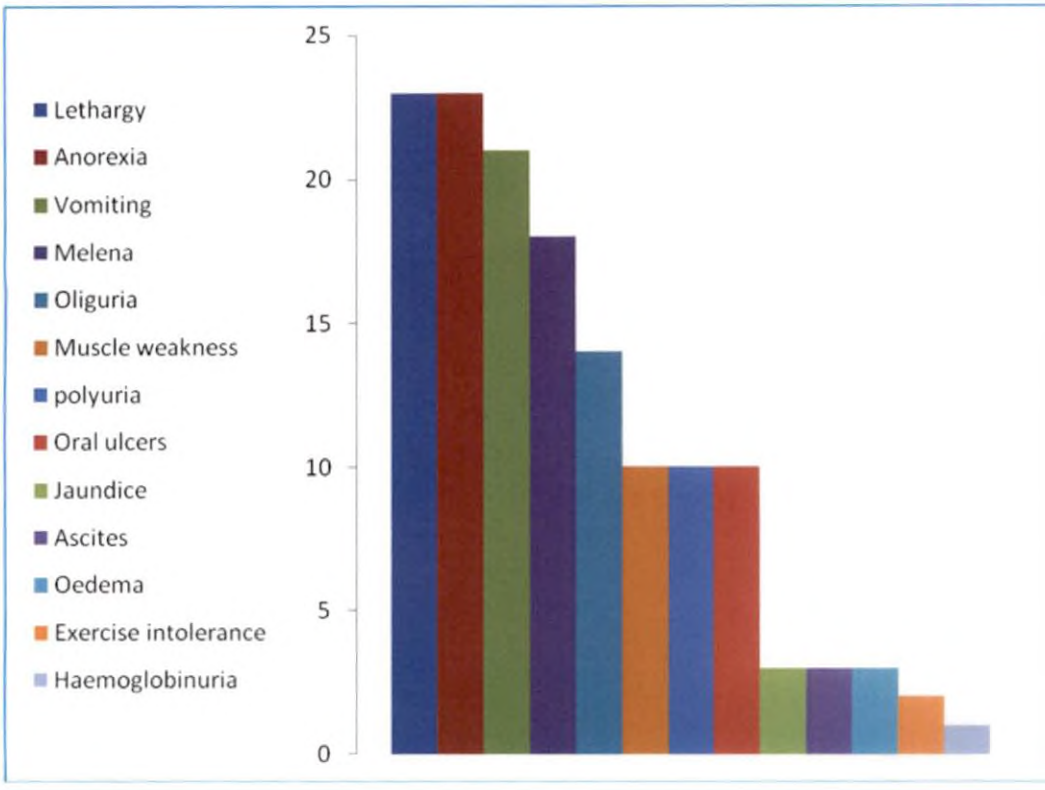
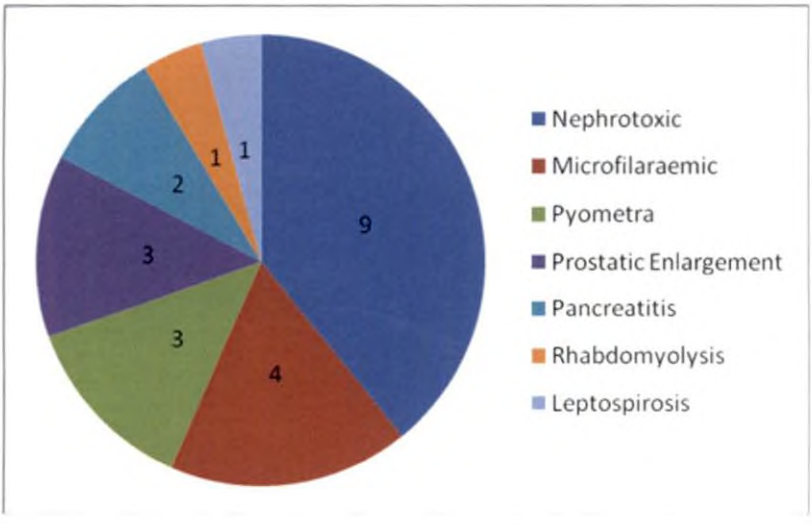


Fig.6: Classification



anuria or oliguria(61%), weakness(43%), polyuria (43%),oral ulcers(43%), jaundice, ascites, oedema (13%), exercise intolerance(8%), and haemoglobinuria (4%).(Fig.5)

Analysis of history revealed that nine dogs had exposure to nephrotoxic drugs (39%), four animals were microfilaraemic (17%), three each had pyometra or enlargement of prostate gland (13%), two had pancreatitis(9%), and one each had rhabdomyolysis or leptospirosis.(4.5% each). The sick animals were grouped based on clinicopathological findings and anamnesis. (fig.6)

4.1 RENAL FAILURE ASSOCIATED WITH NEPHROTOXIC DRUGS:

Clinical examination revealed that majority of the animals were dehydrated and fluid therapy was not given many a times before giving anti-inflammatory or antibiotic therapy. Nephrotoxic instances observed were prolonged and simultaneous treatment with ivermectin and oxytetracycline,(1) combined treatment with oxytetracycline and meloxicam (2), gentamicin and meloxicam (1) gentamicin (2) ceftriaxone (2) and meloxicam(1).

4.1.1 Signalment

Age:

The mean age of dogs affected with renal failure in this group was 7.48 years with a range of 4 months to 13 years. There was a dog below four years,

three dogs in the age group of 4-8 years, four dogs in the age group of 8-12 years and one dog in the age group of more than twelve years. Maximum numbers of cases were recorded in the age group of 8-12 years followed by 4-8 years.

Breed

Out of the nine dogs affected with renal failure, five were German shepherd dogs, two were nondescript, and one each was Rottweiler and Neapolitan mastiff.

Sex

There were five male dogs and four female dogs in the selected group.

Vaccination status

Eight dogs were vaccinated against rabies and six were vaccinated with multicomponent vaccine.

4.1.2 Clinical Observations

The mean body temperature on the day of admission was 101.37 ± 0.47 °F, pulse was 99.30 ± 5.39/min and respiration was 23.60 ± 1.59/min. The visible mucous membranes were pale in six cases, pale roseate in two and congested in one.

All the dogs in this group were showing signs of lethargy and anorexia, nine dogs had vomiting, oedema was seen in two, jaundice in one, oral ulcers in four, oliguria in seven, polyuria in three and muscle weakness in two.

4.1.3 Clinical pathology

Haemogram:

The mean haemoglobin, total erythrocyte count, volume of packed red cells and erythrocyte sedimentation rate in healthy dogs were 14.033 ± 0.80 g% , 7.017 ± 0.46 millions./mm^3, 38.13 ± 2.89 % and 10.67 ± 2.19 mm/hr respectively. The mean values shown by diseased dogs on the day of admission were haemoglobin 8.88 ± 0.88 g%, total erythrocyte count 4.11 ± 0.46 millions /mm^3 ,volume of packed red cells 27.06 ± 2.87% and erythrocyte sedimentation rate 28.8 ± 12.68 mm/hr.

The corresponding values on 7^{th} day were 8.21 ± 1.36 g%, 3.50± 0.74 millions /mm^3, 23.53 ± 3.97% and 35 ± 18.13 mm/hr. Statistical analysis did not reveal any significant difference between the pre and post treatment values of haematological parameters.(Table.1)

Leucogram:

Mean total leucocyte count (TLC), percentage of neutrophils, lymphocytes and eosinophils in healthy animals were 13900 ± 516.40 / mm^3, 77.17 ± 1.94, 21.83 ± 4.58 and 1 ± 0.33 % respectively. The mean values of the affected group on the day of admission were 19166 ± 3779.4/ mm^3, 77.90 ± 3.11%, 17.50 ± 2.41%, 2.88 ± 0.85%, and monocytes 5.75 ± 0.85 %. Leucogram on seventh day showed TLC of 20833.33 ± 2453.25/ mm^3, neutrophil percentage of 80.33 ± 3.75, lymphocyte percentage of 14.83 ± 2.34, eosinophil percentage of 3.66 ± 1.68 and monocyte percentage of 5.00 ± 2.00. None of the values showed any statistically significant variation between first and seventh days. (Table.2)

Platelet count:

The mean platelet count of healthy dogs were 373000 ± 38950 / mm^3.In dogs with renal failure having previous exposure of nephrotoxic drugs , mean platelet count on day of admission was 250200 ± 33622.02/ mm^3. On seventh day it was 254800 ± 37764.27/ mm^3. On statistical analysis, no significant variation was found between the values on first and seventh days (Table.2).

Serum biochemical analysis:

Total Protein, Albumin, and Globulin and A: G ratio:

The serum total protein, albumin, globulin and AG ratio in healthy dogs were 5.85 ± 0.22g/dl, 2.16 ± 0.12g/dl, 3.69 ± 0.16g/dl and 0.60 ± 0.04 respectively. The dogs with renal failure on the day of admission were having mean total protein of 7.01 ± 0.29 g/dl, mean albumin 2.35 ± 0.25 g/dl, and mean globulin 4.66 ± 0.27 g/dl. The mean A: G ratio in these animals on the day of admission was 0.52 ± 0.069. The mean total protein, albumin, and globulin and A: G ratio on the 7^{th} day were 7.43 ± 0.84 g/dl, 2.70 ± 0.50g/dl, 4.96 ± 0.35g/dl and 0.56 ± 0.17 respectively. The values on first and seventh days were not significantly different on statistical analysis. (Table.3)

Serum Creatinine:

The mean serum creatinine levels in healthy animals were 0.33 ± 0.09 mg/dl. In the affected group on the day of admission it was 13.15 ± 2.87 mg/dl. On the seventh day mean serum creatinine levels increased to 19.51 ± 2.99 mg/dl. The difference was not statistically significant. (Table.4)

Blood Urea Nitrogen:

The mean blood urea nitrogen (BUN) levels in healthy dogs were 16.29 ± 3.46 mg/dl. In dogs having renal failure, BUN level on the first day was 219.80 ± 55.12 mg/dl and on the seventh day it was 285.00 ± 114.77 mg/dl. On statistical analysis, the 1st and 7th day values were not significantly different. (Table.4)

Serum γ Glutamyl transpeptidase(GGT):

Mean serum GGT level in healthy dogs was 6.25 ± 1.02 IU/L. Corresponding values on day 1 and day 7 in affected dogs were 18.25 ± 7.62 and 25.75 IU /L respectively. The variation between day 1 and day 7 values were statistically not significant. (Table.5)

Serum Potassium:

Mean serum potassium level in normal animals was 4.1 ± 1.56 mEq/L. In dogs with renal failure it was 6.35 ± 1.86 on the first day and 6.11 ± 1.29 m Eq/L on the seventh day. There was no significant difference on statistical analysis. (Table.5)

Urinalysis:

Presence of protein and specific gravity of urine was measured using uristix dipstick test and urine protein was detected on an average of 3+. The mean specific gravity found was 1.0129 ± 0.001 and 1.0150 ± 0.002 on first and seventh day respectively. (Table.4)

Urine protein Creatinine Ratio:

The mean value of urine protein creatinine ratio in normal healthy animals was 0.38 ± 0.05.The value on first day of diseased group was 4.50 ± 0.54 and on the seventh day it was 3.83 ± 0.93.There was statistically significant difference between the values of healthy and affected dogs, but not between 1st and 7th day values of affected dogs. (Table.4)

N-Acetyl-β-D-Glucosaminidase (NAG):

Mean NAG activity in healthy dogs was 7.08 ± 1.00 U/g of creatinine. Mean NAG activity in dogs with renal failure was 69.22 ± 31.93 on the day of admission. There was statistically significant variation between these values. (Table.4)

γ Glutamyl transpeptidase (GGT)

The mean values of urinary GGT were 1.02 ± 0.42 IU/m mol of creatinine in healthy group. In the affected group it was 14.12 ± 9.16 IU/m mol of creatinine. The difference is statistically significant. (Table.4)

Alkaline Phosphatase (ALP)

The mean values of ALP were 5.78 ±1.57 IU/mmol creatinine in healthy dogs. In the clinical cases it was 63.11 ± 32.40 IU/mmol of creatinine which had statistically significant variation with value of healthy dogs. (Table.4)

Ultrasonography

Ultrasonographic examination of seven dogs with renal failure due to exposure to nephrotoxic drugs revealed hyperechoic kidneys with no corticomedullary distinction. Thinning of cortical area was noticed in one dog. One dog had hypoechoic kidneys with reduced corticomedullary distinction and in

another dog kidney showed normal echotexture. Liver with focal hyperechoic areas were seen in two dogs. Prostate was hyperechoic and slightly enlarged and bladder was with urine containing hyperechoic particles in one dog.

4.1.4 Treatment and response to treatment

All the animals were treated with fluids, antibiotics (Inj Amoxycillin Cloxacillin @ 20 mg/kg BW IV twice daily), diuretics(Inj Furosemide @ 2 mg/kg BW), antiemetics(Inj Metoclopramide @ 0.2-0.4 mg/kg BW SC four times daily), antiulcer drugs (Inj Pantoprazole @ 1 mg/kg BW IV once daily) and other symptomatic therapy as the condition warranted. Hyperkalaemic animals were treated with insulin @ 0.25-0.5 U/kg IV and dextrose 25%(1-2 g IV per unit of insulin given) injection or calcium gluconate 10% solution @ 0.5-1.5 ml/kg intravenously. In three cases clinical improvement was shown by the animals for the first two days thereafter the condition worsened. None of the animals responded favorably to the treatment. One of the animals died on the same day of admission, one on the second day, and one on fifth day. Only one animal survived for more than one month which also died before completing two months. All the other animals survived till the observation period of seven days, but died within one month.

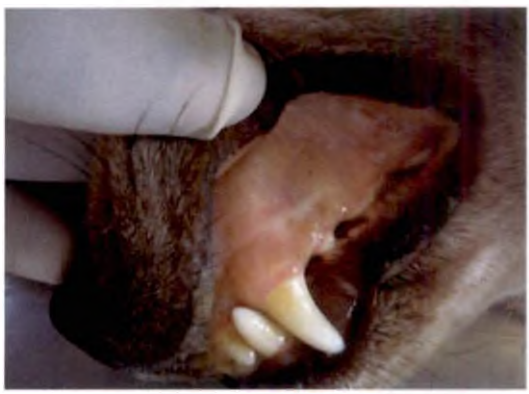
Five animals which did not respond to routine therapy were subjected to peritoneal dialysis. The blood urea nitrogen and serum creatinine values of these animals prior to dialysis and after dialysis are presented in table 11.

4.1.5 Postmortem and Histopathological Examination:

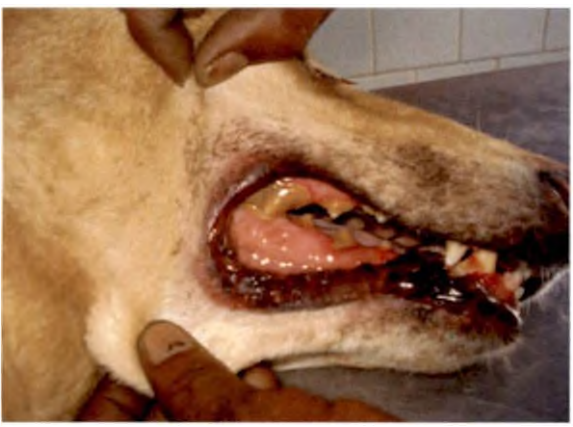
Postmortem examination of two animals only could be conducted. The kidneys were contracted, pale with irregular shape pitting on the surface. The other lesions were haemorrhages in bladder and haemorrhagic gastroenteritis. One animal had bilateral hypertrophy of heart and oedema of lungs.

Plate.2: Nephrotoxic Group- Clinical signs and Ultrasonography

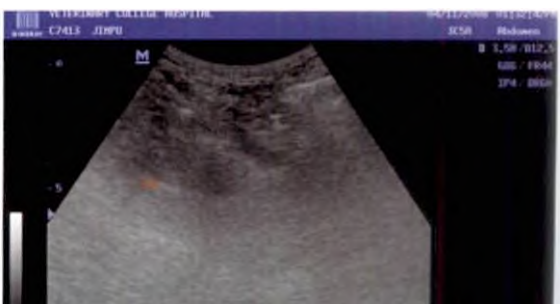
A:Lethargy



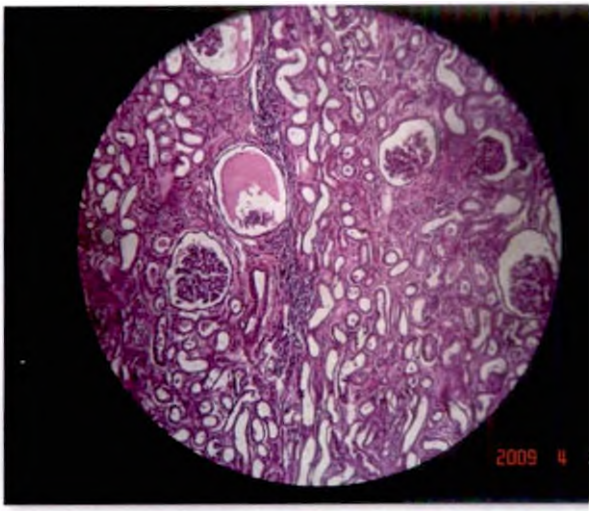
B: Jaundice



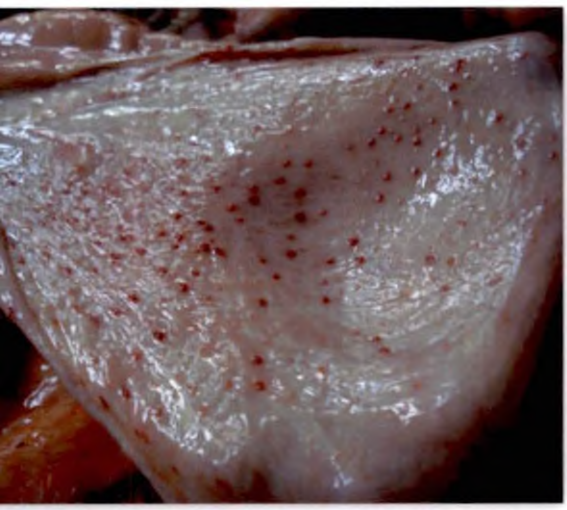
C: Oral Ulcers

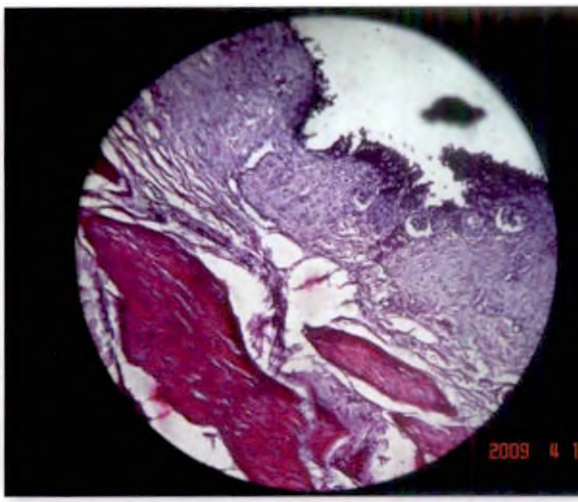


3:Nephrotoxic Group-Postmortem and Histopathology

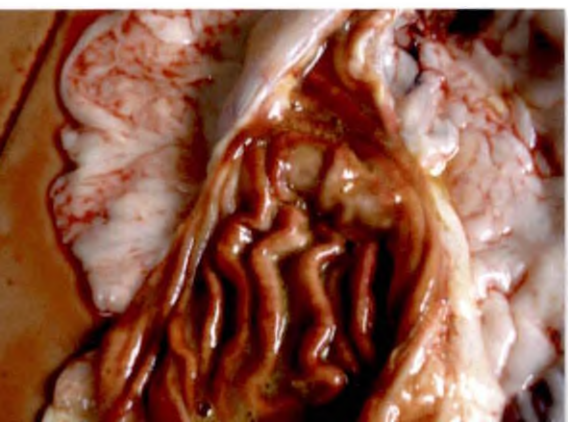


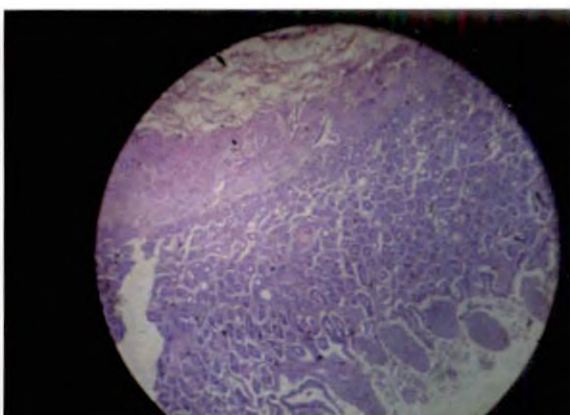
tracted Kidneys (Gross) and histopathology





emorrhage -Urinary Bladder gross and histopathology





Histopthological observations were interstitial and glomerular fibrosis, atrophy, vascular sclerosis with thrombosis, inflammatory cell infiltration in the interstitium, cystic dilatation of tubules and hyaline casts in the lumen of some of the tubules.

4.2 RENAL FAILURE ASSOCIATED WITH MICROFILARAEMIA

Four cases were classified as renal failure associated with microfilaraemia. All the four dogs were referred cases with complaint of anorexia and vomiting for considerable duration. Wet film examination of these animals showed 5+,3+,3+and 2+ levels of microfilaraemia.

4.2.1 Signalment

Age

Mean age of affected dogs was 6.5 years with a range of 5-8 years.

Breed

The breeds affected were Nondescript (n=2), German shepherd(n=1) and Dalmatian(n=1).

Sex:

All affected dogs were males.

Vaccination status:

Three dogs were vaccinated against rabies and two with multicomponent vaccine.

4.2.2 Clinical Observations:

The mean temperature, pulse and respiration rates of microflaraemic dogs were (range in parenthesis) 101.3°F (100-103), 89.75/min (70 -115) and 21/min(20-24) respectively.

Visible mucous membranes were pale in two animals and congested in the other two. Two animals were showing hind limb weakness, one dog had conjunctivitis and another had skin lesions. Lethargy, vomiting and anorexia were seen in all the dogs. Polyuria and muscular weakness were seen in two dogs and oliguria and oral ulcers in one dog each.

4.2.3 Clinical pathology

Haemogram

The mean haemoglobin concentration, total erythrocyte count, packed cell volume and erythrocyte sedimentation rate on the day of admission were 10.15 ± 2.08 g%, 5.70 ± 0.89 millions./mm^3,29.60 ± 6.55 %, and 61.50 ± 32.04 mm/hr respectively. Corresponding values on day 7 were 11.83 ± 2.47 g%, 5.57 ± 1.19 millions /mm^3, 34.06 ± 7.65 % and 47.66 ± 41.28 mm/hr respectively.(Table.6)

Leucogram:

The mean total leucocyte count on the first day was 15925 ± 3699.40/ mm^3, neutrophil, lymphocyte, eosinophil and monocyte count were 74.75 ± 5.73, 18.50 ± 2.90%, 4.75 ± 3.11 %, and 2.66 ± 0.88 % respectively. The corresponding values on seventh day were 20400 ± 5146.84/mm^3, 78.66 ± 2.90 %, 16.25 ± 2.05 %, 3.00 ± 0.81 and 2.50 ± 1.50 % respectively. (Table.6)

***Platelet Count*:**

The mean platelet count on the first day was 297000.00 ± 87135.90 and it increased to 407333.33 ± 137787.67 on the seventh day.(Table.6)

Serum biochemical analyses:

Total Protein, Albumin, Globulin and A: G ratio:

Total protein, albumin, globulin and AG ratio values on the first day (with seventh day values in parenthesis) were 8.22 ± 0.24 g/dl (8.36 ± 0.18 g/dl), 2.30 ± 0.10 g/dl (1.94 ± 0.41 g/dl), 5.92 ± 0.30 g/dl (6.41 ± 0.24 g/dl) and 0.39 ± 0.02 (0.31 ± 0.04) respectively.(Table.6)

***Serum Creatinine*:**

The mean serum creatinine level on the day of admission was 10.79 ± 2.72 mg/dl while that of seventh day was 8.43 ± 3.47 mg/dl.(Table.6)

Blood urea Nitrogen:

Mean blood urea nitrogen level of affected dogs on first day was 216.75 ± 79.97 mg/dl while that of seventh day was 173.74 ± 79.05 mg/dl.(Table.6)

Serum GGT:

Serum GGT on day of presentation was 14.07 ± 2.69 IU/L while that of seventh day was 9.00 ± 2.13 IU/L. (Table.6)

Serum Potassium:

Mean serum potassium level on first day was 4.42 ± 0.37m Eq/L and that of seventh day was 4.35 ± 0.38 m Eq/L(Table.6)

Urinalysis:

Urine protein was detected on an average of 2+.The mean specific gravity was 1.0125 ± 0.002 and 1.0117 ± 0.001 on first and seventh day respectively. Microscopical examination of urinary sediments revealed crystals of triple phosphate and pus cells in normal limits.

Urine protein Creatinine Ratio:

Mean value of urine protein creatinine ratio on first day of diseased group was 4.44± 1.91 and on the seventh day it was 7.99 ± 2.60.(Table.6)

N-Acetyl-β-Glucosaminidase (NAG):

Level of urinary NAG was measured in two dogs and the values were 15.99 U/g of creatinine and 50.91 U/g of creatinine on the day of admission. (Table.6)

***γ Glutamyl trandpeptidase (GGT)*:**

Urinary GGT was measured only in two dogs in this group and the values were 3.67 IU/m mol and 7.13 IU/mmol of creatinine(Table.6).

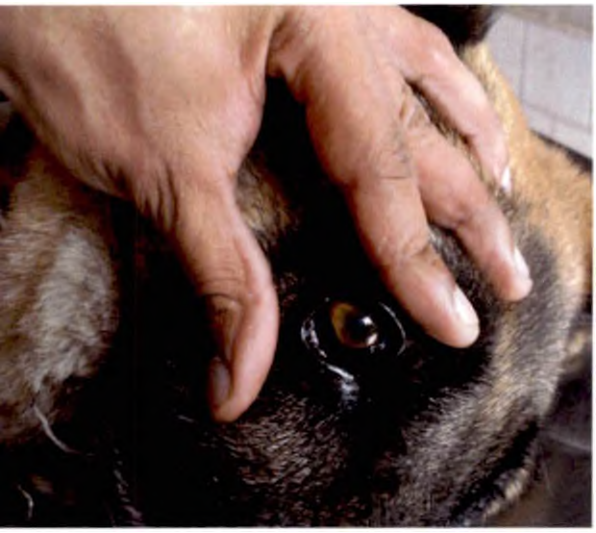
Alkaline Phosphatase (ALP) :

Values of ALP was examined in two dogs and they were 54.29 IU/ mmol and 44.25 IU/ mmol of creatinine.(Table.6)

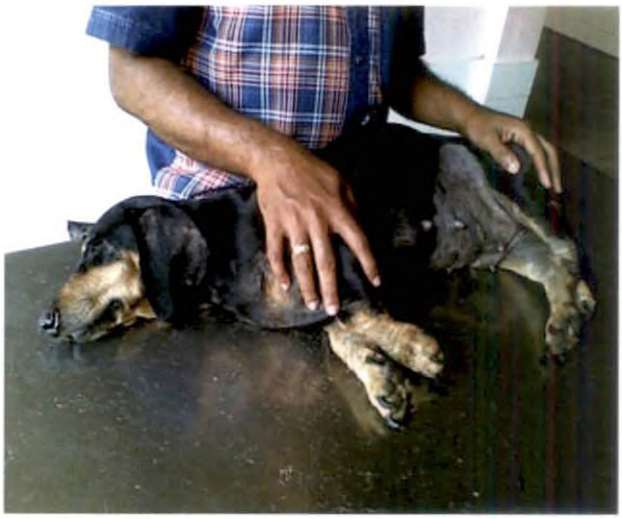
Ultrasonography:

Three animals showed hyperechoic kidneys with no corticomedullary distinction.One animal had hypoechoic cortex with reduced

re.4: Microfilaraemic dogs



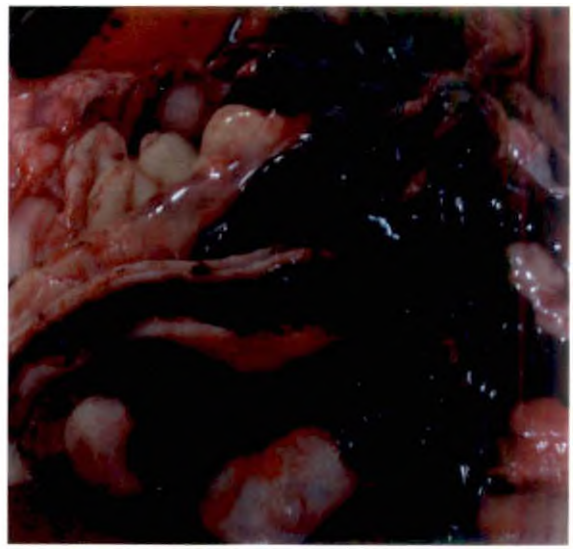
Conjunctivitis



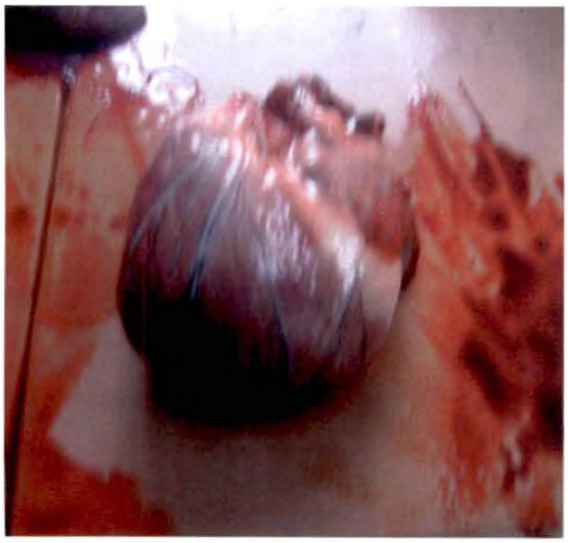
B: Skin lesions

Plate.5: Microfilaraemic dogs-Postmortem Examination.

A:Granular contracted kidneys



B:Haemorrhagic Gastroenteritis



C:Cardiac hypertrophy and dilatation

corticomedullary definition and focal hyperechoic areas in pelvis.Liver had mixed echogenic regions in one dog and in another diffuse hyperechoic areas.

4.2.4 Treatment and response to treatment :

All the dogs were treated with ivermectin injection @ 200 µg/Kg body weight subcutaneously and the dogs became nonmicrofilaraemic on the next day itself. But there was no clinical improvement and all the dogs died , three during the course of treatment and one dog died after one month of discharge.

4.2.5 Postmortem and Histopathological Examination:

Postmortem examination of one animal was conducted. The gross lesions were granular contracted kidneys, severe haemorrhagic gastroenteritis, and cardiac hypertrophy and dilatation..

Histopathologial examination of kidneys showed interstitial nephritis,with widening of interstitium and mononuclear cell infiltration, extensive tubular and glomerular necrosis, hyalinization and calcification of tubules cystic dilatation of tubules and interstitial oedema.

4.3 RENAL FAILURE ASSOCIATED WITH PYOMETRA

Three female nulliparous dogs with signs of pyometra were diagnosed as renal failure cases during the course of treatment.

4.3.1 Signalment

Age:

Mean age of affected dogs was 9 years with range of 7-11 years.

Breed:

The breeds affected were Doberman (*n*=1), Nondescript (n=1) and Labrador (n=1)

Sex:

All affected dogs were females.

Vaccination status:

All three dogs were vaccinated against rabies and two with multicomponent vaccine.

4.3.2 Clinical Observations:

The mean temperature, pulse and respiration rates of dogs were (range in parenthesis) 102.33°F (101.6-103), 106.66/min (100 -120) and 24.33/min(22-26).

Visible mucous membranes were pale in two animals and congested in the other one. Lethargy, vomiting and anorexia were seen in all the dogs and oliguria and melena in two.

4.3.3 Clinical pathology

Haemogram:

The mean haemoglobin concentration, total erythrocyte count, packed cell volume and erythrocyte sedimentation rate on the day of admission with range shown in brackets were 7.67g% (4.8-10.5), 3.40 millions./mm^3(1.72-5.14), 23.70 % (15.4-32.8), and 74.50 mm/hr (15-134) respectively. The corresponding values on

seventh day were 7.90 g%(6.4-9.4), 3.65millions./mm^3 (2.9-4.4), 24.40 %(19.5-29) and 82.50 mm./hr(45-120) (Table.7)

Leucogram:

The mean and range of total leucocyte count on the first day was 25433.33/ mm^3(9400-33800), neutrophil count 72.33 % (67-75), lymphocyte count 20.33 % (20-21), eosinophil count 3.33 %(1-5), and monocyte count 12%.(one sample only). The corresponding values on seventh day were 17650/mm^3 (11300-24000), 69.5 % (65-74), 20.33 (20-21) %, 3.33 (1-5) and 8.50 % (6-11) respectively (Table.7).

Platelet Count:

The mean platelet count on first day, 171000 (98000-242000) increased to 201000 (one value only) on the seventh day (Table.7)

Serum biochemical analysis:

Total Protein, Albumin, Globulin and A: G ratio:

Total protein, albumin, globulin and AG ratio values on the day of admission (with range of values in parenthesis) were 7.5 g/dl (6.8-8.7), 2.47 g/dl(2.3-2.7), 5.03 g/dl (4.1 – 6.4 g/dl) and 0.53 (0.4-0.7) respectively. On the seventh day the values were 8.00 g/dl(one value only), 2.00 g/dl(one value only), 6.00 g/dl(one value only) and 0.33(one value only) respectively (Table.7).

Serum Creatinine

The mean serum creatinine level on the day of admission was 10.90 mg/dl (6.1-15) while that of seventh day was 9.75 mg/dl (4.2-15.3) (Table.7).

Blood urea Nitrogen

Mean blood urea nitrogen level of affected dogs on first day was 133 mg/dl (78-190) while that of seventh day was 84.50 mg/dl (59-110). (Table.7)

Serum GGT

Serum GGT on first day was 9.0 (8-10) IU/L while that of seventh day was 8.67 IU/L (7-10). (Table.7)

Serum Potassium

Mean serum potassium level on first day was 5.7mEq/L and that of seventh day was 6.6 mEq/L. (Table.7)

Urinalysis

Presence of protein in urine and urine specific gravity was measured using uristix dipstick test.

Urine protein was detected on an average of 3+. The mean specific gravity was 1.010 (Table.7).

Urine protein Creatinine Ratio

Mean value on first day was 8.60 and the range was 5.5-11.7. (Table.7)

N-Acetyl-β-D-Glucosaminidase (NAG):

Level of urinary NAG was measured in two dogs and the values were 125.94 U/g of creatinine and 180.72 U/g of creatinine on the day of admission. (Table.7)

γ Glutamyl transpeptidase (GGT) :

Urinary GGT was measured in two dogs only in this group and it was found to be 32.39 IU/m mol and 82.48 IU/mmol of creatinine. (Table.7)

Alkaline Phosphatase (ALP) :

Values of ALP were examined in two dogs and they were 30 IU/ mmol of creatinine and 324.66 IU/ mmol of creatinine. (Table.7)

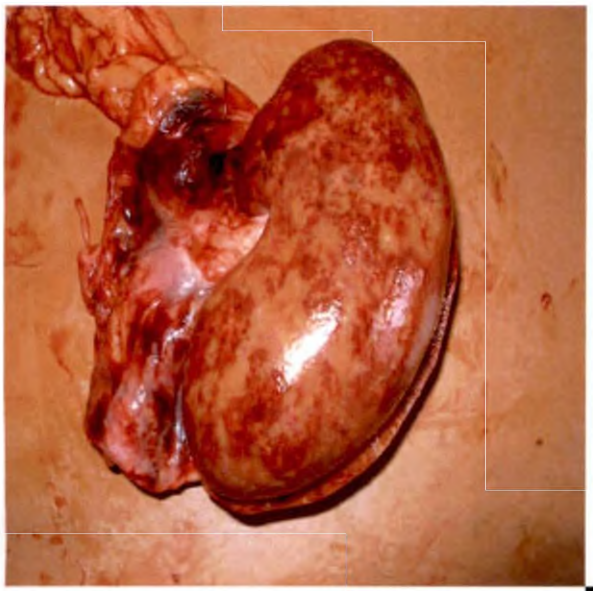
Ultrasonography:

One dog was with kidneys of normal echogenicity .In another dog, enlarged hyperechoic uterus, hypoechoic kidneys and enlarged spleen could be visualized. Medullary rim sign could also be visualized in this dog. In the third dog, hyperechoic kidneys with reduced corticomedullary distinction and hyperechoic diffuse areas in liver could be noticed.

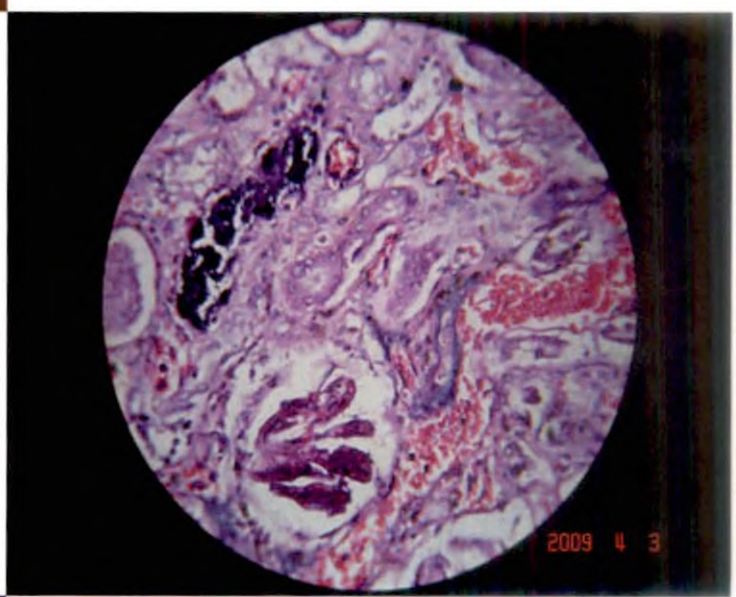
4.3.4 Treatment and response to treatment :

All the animals were treated with fluids, antibiotics (Inj Amoxycillin Cloxacillin @ 20 mg/kg BW IV twice daily), diuretics(Inj Furosemide @ 2 mg/kg BW), antiemetics(Inj Metoclopramide @ 0.2-0.4 mg/kg BW SC four times daily),

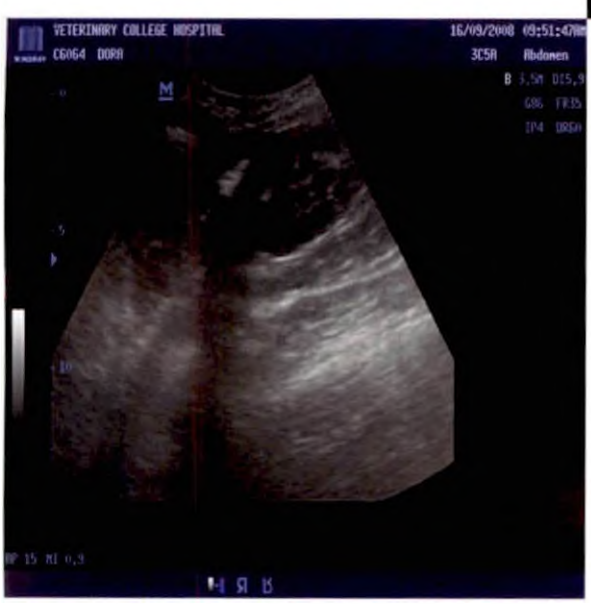
Plate.6: Dogs with pyometra



A:Kidney-Gross



Kidney-Histopathology
Haemorrhage and calcification



C:Kidney Ultrasonogram-
Medullary rim sign

antiulcer drugs (Inj Pantoprazole @ 1 mg/kg BW IV once daily) and other symptomatic therapy as the condition warranted.None of the dogs survived as the lesions in kidney were too advanced.

4.3.5 Postmortem and Histopathological Examination:

PM examination of one dog was done. Kidneys were small with granular and depressed surface. Cortical area was shrunken. Liver was hard and fibrotic with occasional nodules on the surface. Haemorrhagic gastro enteritis and haemorrhages in the bladder could also be detected. The kidney lesions on examination revealed characteristic glomerular and tubular sclerosis, cystic dilatation of tubules, multifocal haemorrhage, glomerular haemorrhage and mononuclear cell infiltration.

4.4 RENAL FAILURE ASSOCIATED WITH PROSTATIC ENLARGEMENT

Three dogs with enlargement of prostate and consequent obstruction of urine outflow developed postrenal renal failure.

4.4.1 Signalment

Age

Mean age of affected dogs was 9.33 years (6-13 years)

Breed

The breeds affected were German shepherd (n=2) and Spitz (n=1)

Sex

All affected dogs were males.

Vaccination status

All three dogs were vaccinated against rabies and two with multicomponent vaccine.

4.4.2 Clinical Observations

The mean temperature, pulse and respiration rates of dogs were (range in parenthesis) 101.6°F (100.8-102), 110/min (90 -120) and 24 /min (20-28).

Visible mucous membranes were pale, pale roseate and congested in one animal each. Lethargy, oliguria, vomiting, muscle weakness and anorexia were seen in all the dogs and melena in two.

4.4.3 Clinical pathology

Haemogram

The mean haemoglobin concentration, total erythrocyte count, packed cell volume and erythrocyte sedimentation rate on the day of admission with range shown in brackets were 11.07g % (6.9-14.5), 6.39 mill./mm^3 (6.38-6.4), 43.25 % (41.5-45), and 28.5 mm/hr (2-55) respectively. The values on seventh day were haemoglobin 9.00 g% (3.00-15.4), erythrocyte count 6.47mill./mm^3 (6.2-6.74), packed cell volume 37.10 % (33 – 41.2) and erythrocyte sedimentation rate 41.5 mm./hr (3-80) . (Table.8)

Leucogram

The mean total leucocyte count on the first day was 20025.00/ mm^3 (12700-27350), neutrophil count 76.50 % (76-77), lymphocyte count 21.50 % (21-22) eosinophil count 2 % (2), and monocyte count 0 % (0). The corresponding values on seventh day were 32450/mm^3 (32300-32600), 79 % (79-79), 19 (19-19) %, 2 (2-2) and 0 % (0) respectively. (Table.8)

Platelet Count

The mean platelet count on first day was 180666.67(152000-198000) and the value increased to 193000 (180000-206000) on the seventh day. (Table.8)

Serum biochemical analysis

Total Protein, Albumin, Globulin and A:G ratio

Total protein, albumin, globulin and AG ratio values on the first day (with range of values in parenthesis) were 7.87 g/dl (6.5-8.87), 2.31 g/dl (2.1-2.7), 4.98 g/dl (3.8-6.15 g/dl) and 0.52 (0.34-0.7) respectively. On the seventh day they were 7.5 g/dl (6.8-8.2), 2.35 g/dl (2.00-2.70), 5.15 g/dl (4.1-6.2) and 0.51 (0.32-0.7). (Table.8)

Serum Creatinine

The mean serum creatinine level on the day of admission was 16.33 mg/dl (11.00-18.80) while that of seventh day was 16.08 mg/dl (11.06-21.10). (Table.8)

Blood urea Nitrogen

Mean blood urea nitrogen level of affected dogs on first day was 162.33 mg/dl(120-216) while that of seventh day was 241.90 mg/dl (191 -292.80). (Table.8)

Serum GGT

Serum GGT on first day was 11.75 (5.5-18) IU/L while that of seventh day was 17.57 IU/L (11-24). (Table.8)

Serum Potassium

Mean serum potassium level on first day was 4.45m Eq/L (4.3-4.6) and that of seventh day was 4.55 m Eq/L (4.3-4.8). (Table.8)

Urinalysis

Urine protein was detected on an average of 4+.The mean specific gravity was 1.010 (Table.8).

Urine protein Creatinine Ratio

Mean value on first day was 3.57 and the range was 2.6-4.53 (Table.8)

N-Acetyl-β-Glucosaminidase (NAG)

Level of urinary NAG was measured in two dogs and the values were 456.44U/g and 21.14 U/g of creatinine on the day of admission. (Table.8)

γ Glutamyl trandpeptidase (GGT)

Urinary GGT was measured in two dogs only in this group and the values were 34.12 IU/m mol and 2.01 IU/mmol of creatinine. (Table.8)

Alkaline Phosphatase (ALP)

Values of ALP were recorded in two dogs and they were 17.14 IU/ mmol of creatinine and 10.71 IU/ mmol of creatinine (Table.8).

4.4.4 Ultrasonography

Kidney cortex was thick and hyperechoic in one dog and right kidney was affected more Hyperechoic area within the bladder with shadowing was seen in the same dog. Hyperechoic kidney with reduced corticomedullary distinction in another dog and hypoechoic kidney with hyperechoic areas in both renal pelvis. In all dogs prostate was enlarged.

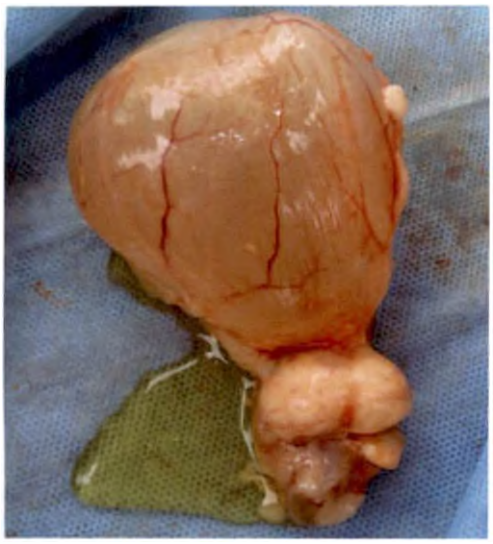
4.4.5 Treatment and Treatment Response

Symptomatic treatment with fluids, antibiotics, diuretics and antiemetics attempted, but all the animals succumbed.

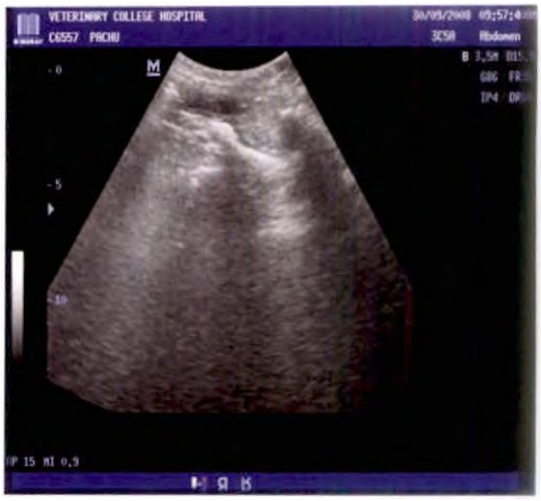
4.4.6 Postmortem and Histopathological Examination

Post mortem examination of all the three animals was conducted. In one animal both kidneys were small, haemorrhagic and irregular with both renal pelves containing renoliths. Bladder was distended with urine and bladder wall was thin. Enlarged prostate obstructing the flow of urine was detected..An enlarged subcutaneous mass in perineal region covered by muscular walls was also detected. Right atrial enlargement and hemorrhagic gastroenteritis were also observed. In the

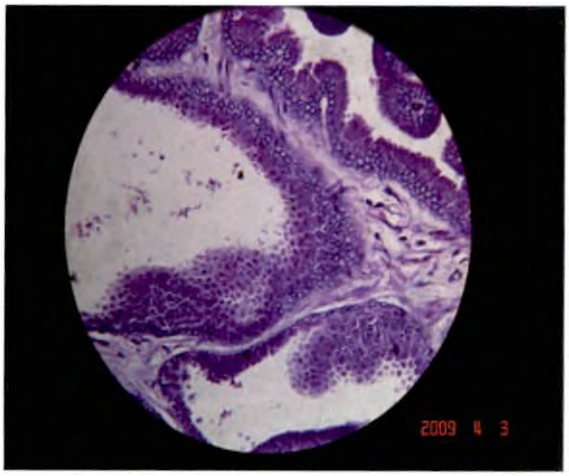
Plate.7: Dogs with prostatic enlargement



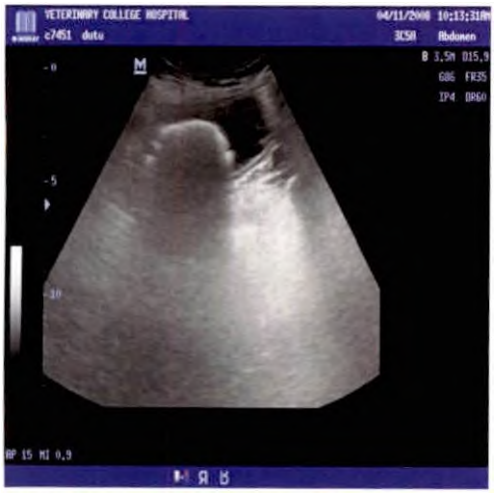
A:prostatic enlargement



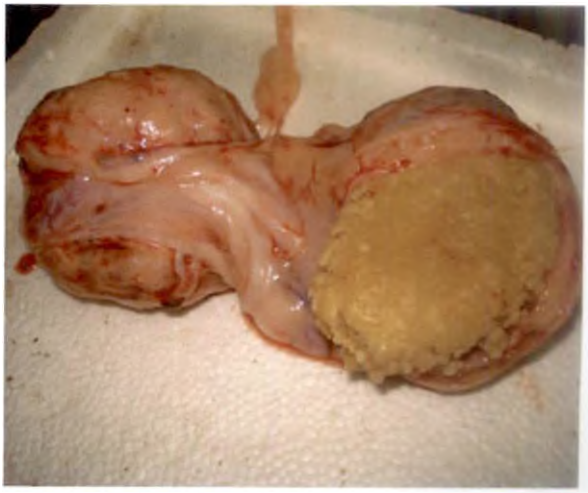
B:Prostatic enlargement-
Ultrasonogram



C:Prostatic hyperplasia and hypertrophy
Histopathology



D:Urolith in bladder-
Ultrasonogram



E:Urolith in bladder with
enlargement of prostate

second animal bladder was filled with urine. Neck of bladder was obstructed by enlarged prostate with inspissated pus. Both kidneys were small and hemorrhagic and irregular in shape. Post mortem examination of third animal revealed small, round and contracted pale kidneys Prostate was enlarged. Urinary bladder was rounded and contained a large stone obstructing the outflow of urine. Liver was hard and nodular.

Histopathology of kidneys revealed glomerular and tubular necrosis, extensive interstitial and intratubular haemorrhage, widening of interstitium, cystic changes, calcification of the tubules, focal infiltration of inflammatory cells, hyaline casts in some of the tubules, glomerular haemorrhage and atrophied glomeruli. Histopthological examination of prostate revealed prostatic hyperplasia and diffuse fibrosis.

4.5 RENAL FAILURE ASSOCIATED WITH PANCREATITIS

Two cases of pancreatitis associated with renal failure were investigated.

4.5.1 Signalment:

The dogs were a nine year old nondescript castrated male and ten year old female Labrador.

They were both vaccinated against rabies. Multi component vaccine was given only to the Labrador dog.

4.5.2 Clinical Observations:

The primary complaint of both the dogs was anorexia for a prolonged period (10 and 15 days) and abdominal pain. The temperature, pulse and respiration rates of the

dogs were 100.2 and 102.4 °F, 96 and 100/min , 28 and 20/min respectively.

Visible mucous membranes were pale in both dogs.. Lethargy, oliguria, vomiting, ascites and anorexia were seen in both the dogs and melena and oral ulcers in one. Praying posture was noticed in one dog and purulent discharge from eyes noticed in the other dog.

4.5.3 Clinical pathology

Haemogram:

Haemoglobin 6.00 and 5.1 g %, erythrocyte count 3.06 and 2.8 mill./mm^3,PCV 17.2 and 17 % and ESR 5 and 36 mm/hr were the values on the first day. The corresponding values of seventh day were 6.1 and 4.8 g%, 3.38 and 2.1 mill./mm^3, 19.4 and 18 % and 3 and 40 mm/hr respectively.(Table.9)

***Leucogram*:**

The leucogram of the animals showed total leucocyte count of 13300 and 8700/ mm^3, neutrophil count of 75 and 69 %, lymphocyte count of 20 and 23 %, eosinophil count of 3 and 7 % and monocyte count of 2 and 1 %. On the seventh day these values were 16100 and 6500/ mm^3, 88 and 72 %, 11 and 26%, and 1 and 2 % respectively. Monocytes were not seen on the seventh day. (Table.9)

***Platelet Count*:**

The platelet count on day of presentation was 245000 and 318000/ mm^3. On the 7^{th} day it was 259000 and 305000/mm^3 respectively.

Serum biochemical analysis:

Total Protein, Albumin, Globulin and A:G ratio:

Total protein, albumin, globulin and AG ratio values on the first day (with seventh day values in parenthesis) were 6.2 and 5.12 g/dl (5.8 and 6.42), 2.4 and 1.53 g/dl (2.2 and 1.88), 3.8 and 3.59 g/dl (3.6 and 4.54 g/dl) and 0.6 and 0.42 (0.6 and 0.41) respectively. (Table.9)

Serum Creatinine:

The mean serum creatinine level on the day of admission was 18 and 26 mg/dl while that of seventh day was 14.3 and 18.94 mg/dl. (Table.9)

Blood urea Nitrogen:

Blood urea nitrogen level of affected dogs on first day was 154 and 190 mg/dl while that of seventh day was 132 and 165 mg/dl. (Table.9)

Serum GGT:

Serum GGT on first day was 7.8 and 11 IU/L while that of seventh day was 8.1 and 9.0 IU/L. (Table.9)

Serum Potassium:

Mean serum potassium level on first day was 8.54 and 4.61 m Eq/L and that of seventh day was 8.5 and 6.41 m Eq/L. (Table.9)

Fasting blood glucose was 132 mg/dl for one animal . For the other animal, fasting blood glucose level was consistently high in the range of 120-160 mg/dl. Serum cortisol 7.1mcg/dl, serum phosphorus 20.4 mg/dl, serum lipase 2340

units, serum cholesterol 194 mg/dl, Serum alkaline phosphatase 273 u/l and serum calcium 8 mg% were the other relevant biochemical results

Urinalysis:

Presence of protein in urine and urine specific gravity were measured and urine protein was detected on an average of 3+. The specific gravity were 1.010 and 1.015

Urine protein Creatinine Ratio and Urinary Enzymes:

Urine protein and creatinine ratio on the day of admission was 9.94 and 2.1 and and on seventh day one dog was anuric and UPC of other dog was two. Urinary enzymes were measured for one dog and the value of NAG was 28.21 U/g of creatinine, GGT 18.55 IU/mmol of creatinine and ALP 113.48 IU/mmol of creatinine. (Table.9)

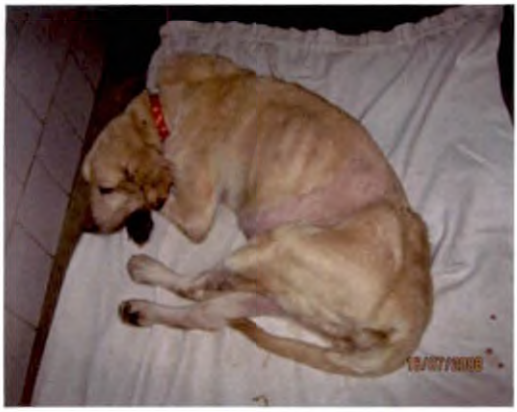
Ultrasonography:

Moderate amount of fluid in abdominal cavity, hypoechoic kidneys with reduced corticomedullary distinction, a hyperchoic mass cranial to kidneys with a localized hypoechoic area in the middle were the important observations in the first dog. In the second dog both kidneys had distorted shape, hyperechoic and with reduced corticomedullary distinction.

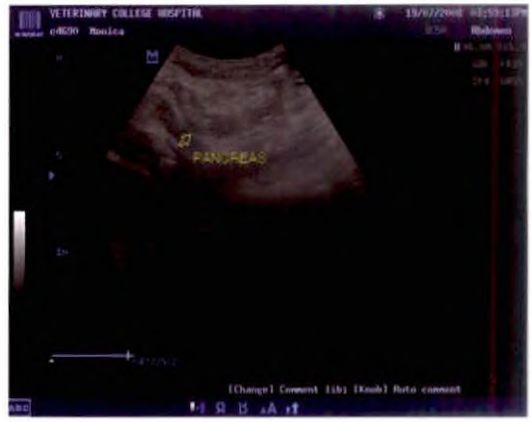
4.5.4 Treatment and Response to Treatment

Treatment with fluids, antibiotics, diuretics and antemetics attempted. All animals succumbed to the advanced renal failure.

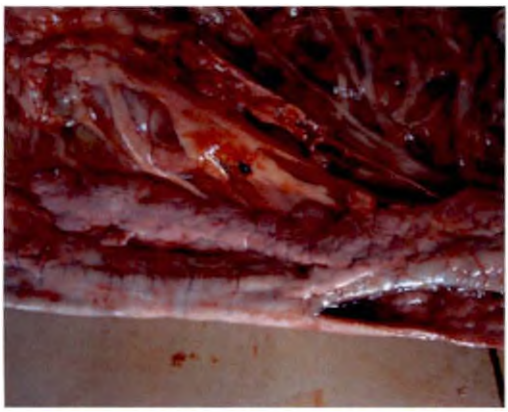
Plate.8: Pancreatitis



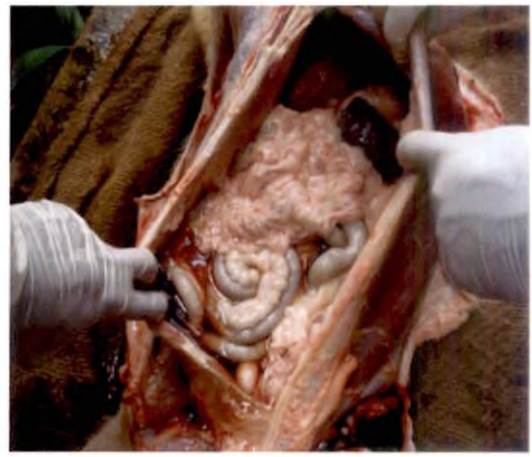
A: Severe abdominal pain



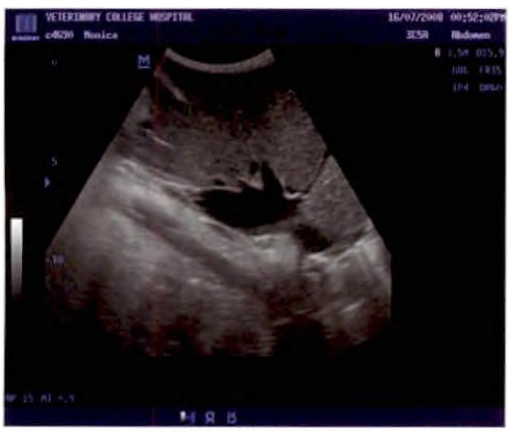
B: Ultrasonogram
Pancreas



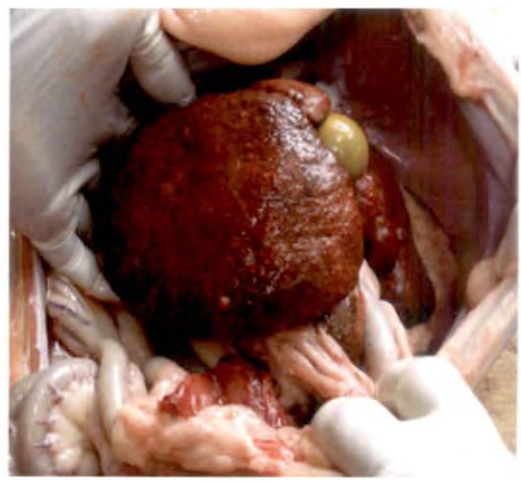
C: Pancreatitis-gross



D: Ascites and enlargement of pancreas



E: Ultrasonogram
Ascites and cirrhosis



F: Cirrhosis-gross

4.5.5 Postmortem and Histopathological examination:

Postmortem examination of both the animals were conducted. In one animal the lesions observed were moderate amount of serosanguinous fluid in the abdominal cavity, enlargement of pancreas with greyish white diffuse nodules, cirrhotic liver, haemorrhagic gastroenteritis, small shrunken and irregular kidneys, pneumonic changes in lungs, fibrinous pericarditis and heamorrhages in bladder.

In the other animal lesions observed were large quantity of serous fluid in pleural cavity with fibrin deposits, collapsed lungs, rounding of heart with hydropericardium, enlargement of left atrium, fibrosis of liver, enlargement of pancreas with areas of calcification, severe haemorrhagic gastroenteritis and small kidneys with haemorrhagic patches.

Histopathological examination showed diffuse lobular-acinar cell necrosis in pancreas and congestion of inter lobular vessels. Islet zone cells were scanty and showed hyalinization of islet zone.

In the kidney sections, diffuse interstitial fibrosis,atrophy and cystic changes of glomeruli, tubular degeneration, necrosis and medullary tubular hyalinization were the lesions observed.

4.6 RHABDOMYOLYSIS:

The case was presented with a history of continous and unusual physical exertion for four hours which afterwards developed acute pain on limbs, later haemoglobinuria and myoglobinuria. It became oliguric, and anorectic. It was diagnosed as acute renal failure following exertional rhabdomyolysis

4.6.1 Signalment:

It was a male weimaraner dog aged three years with a history of regular vaccination.

4.6.2 Clinical observations :

The animal was laterally recumbent. Rectal temperature at the time of presentation was 98 ^{O}F, pulse 96/min and respiration 28/min. The conjunctival mucous membranes were congested. The animal was anorectic and had vomiting and the vomitus was blood tinged. Oliguria also was noticed. Echymotic patches were seen on the body surface and penile mucosa. The animal was dull, lethargic, having haemoglobinuria and myoglobinuria, icterus, oral ulcers, and muscle weakness.

4.6.3 Clinical pathology

Haematology , serum biochemistry and urinalysis:

The haemoglobin percentage, RBC count, PCV percentage and ESR of the animal on the day of admission were 17 g%, 6.87 milllions/cmm, 56.8% and 2mm/hour respectively.

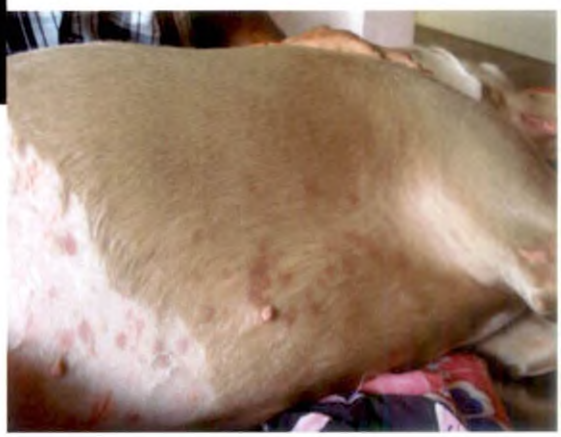
Total leucocyte count was 38600/cmm with differential count of neutrophils 68 %, and lymphocytes 28 %.,Eosinophils 2 % and monocytes 2%.

Platelet count of the animal was 26000/cu mm.

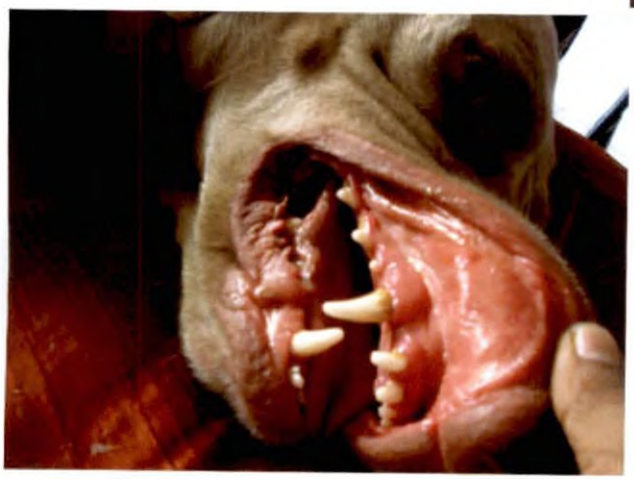
Serum total protein, albumin and globulin were 5.6, 2.7 and 2.9 g /dl respectively. The A:G ratio was 0.7.

Plate.9: Rhabdomyolysis

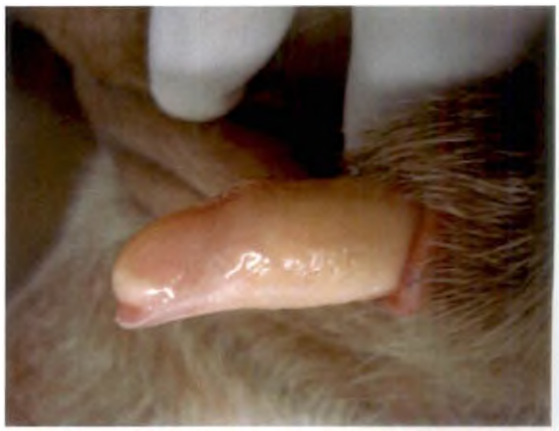
A: Animal



B: Echymotic patches



C: Oral ulcers



D: Icterus-penile mucosa

Serum creatinine was 5.6 mg/dl and BUN 123 mg/dl. Other biochemical parameters were bilirubin 1.4mg/dl, serum alkaline phosphatase 122 u/l, serum potassium 5 mEq/l ,serum GGT 38 IU/L, serum AST 2390 IU/L, serum ALT 1003 IU/L and serum creatine phosphokinase 55000IU/L.

Specific gravity of urine was 1.007 and the urine sample was positive for myoglobin, protein, glucose and bile pigments. (Table.10)

4.6.4 Ultrasonography:

On ultrasound scanning both kidneys were hypoechoic with no corticomedullary distinction.The liver parenchyma was hypoechoic and the gall bladder was shrunken.The portal veins were dilated.

4.6.5 Treatment and response to treatment

The animal was treated with parenteral fluids,Inj amoxicillin and cloxacillin @ 20 mg/kg body weight and Inj calcium gluconate @1 ml/kg body wt I/V.The animal did not respond to the treatment and died on the fifth day of presentation. Postmortem examination could not be conducted.

4.7 LEPTOSPIROSIS

4.7.1 Signalment:

A nondescript male dog aged 1.5 years was presented with a history of continous vomiting. It was not vaccinated with prophylactic antirabies vaccine or multicomponent vaccine.

4.7.2 Clinical observations:

The animal was oliguric, having difficulty to stand up, was having shaking movement of head while standing, had diarrhea since one day, anorectic and lethargic.The temperature was 100.4°F ,pulse 76/min, respiration 24/min and the visible mucous membranes were congested.

4.7.3 Clinical pathology

Haematology , serum biochemistry and urinalysis:

Haemoglobin, erythrocyte count, VPRC and ESR were 10.3g/dl, 6.23 millions/cmm, 32.6 %, and 10mm/hour respectively on the first day and the corresponding values on seventh day were 10.2, 6.6, 31 and 26 respectively.

The total leucocyte count was 64600/cmm, with neutrophils 80%, lymphocytes 15%, eosinophil 1% and monocyte 4 % . Platelet count was 128000/cu mm. On seventh day these values were 72400/cumm, 82%, 15%, 2%, 1% and 242000/cumm respectively.

The total protein, albumin, globulin and AG ratio were 5.3 g/dl, 2.3g/dl, 3 g/dl, 0.76 respectively on the first day. The same parameters on seventh day were 4.27, 1.59, 2.68 and 0.59 respectively.

Serum creatinine was 11.23 mg/dl on first day and 18 mg/dl on seventh day. Blood urea nitrogen was 256 mg/dl and 372 mg/dl on first and seventh day respectively. Serum GGT Values on first and seventh days were 8.2 and 9.34 IU/L respectively. Serum potassium values were 6.4 and 6.8 mEq/L on first and seventh day respectively.

Urinalysis revealed the following results. Specific gravity was 1.010 and 1.015 on first and seventh days. Protein was 3+, and blood was also present moderately. Urine protein creatinine ratio was 13.54 the urinary NAG was 124.16 mu/mg of creatinine, urinary GGT was 4.49 IU/mmol of creatinine and urinary alkaline phosphatase was 42.62 IU/mmol of creatinine. The urine on dark field microscopy showed leptospiral organisms. (Table.10)

4.7.4 Ultrasonography:

On ultrasonography left kidney hyperechoic, right kidney distended and corticomedullary junction was indistinct.

4.7.5 Treatment and response to treatment

The animal was treated with Benzyl Penicillin @ 40,000 IU/kg body weight twice daily as intravenous injection along with parenteral fluids,(Inj Normal Saline IV) and antemetics (Inj Metoclopramide@ 0.2-0.4 mg/kg SC).The animal did not respond and died on the ninth day of admission. Post mortem examination could not be conducted.

Table 1 Haemogram-Nephrotoxic cases (n=9)

Parameter	Healthy dogs	Diseased dogs 1st day	Diseased dogs 7th day
Haemoglobin (g%)	14.033 ± 0.80	8.88 ± 0.88	8.21 ± 1.36
Total erythrocyte count (mill/mm3)	7.017 ± 0.46	4.11 ± 0.46	3.50± 0.74
Volume of packed red cells (%)	38.13 ± 2.89	27.06 ± 2.87	23.53 ± 3.97
Erythrocyte sedimentation rate(mm/hr)	3.00 ± 0.37	28.8 ± 12.68	35 ± 18.13

Table 2 : Leucogram- Nephrotoxic cases

Parameter	Healthy dogs	Diseased dogs 1st day	Diseased dogs 7th day
Total leucocyte count(/mm3)	13900 ± 516.40	19166 ± 3779.4	20833.33 ± 2453.25
Neutrophils (%)	77.17 ± 1.94	77.90 ± 3.11	80.33 ± 3.75
Lymphocytes (%)	21.83 ± 4.58	17.50 ± 2.41	14.83 ± 2.34
Eosinophils(%)	1.00 ± 0.33	2.88 ± 0.85	3.66 ± 1.68
Platelet count(10^3/mm^3)	373 ± 38.95	250.2 ± 33.62	254.8 ± 37.76

Table 3: Protein Profile- Nephrotoxic cases

Parameter	Healthy dogs	Diseased dogs 1st day	Diseased dogs 7th day
Total Protein (g/dl)	5.85 ± 0.22	7.01 ± 0.29	7.43 ± 0.84
Albumin (g/dl)	2.16 ± 0.12	2.35 ± 0.25	2.70 ± 0.50
Globulin (g/dl)	3.69 ± 0.16	4.66 ± 0.27	4.96 ± 0.35
Albumin Globulin (AG) Ratio	0.60 ± 0.04	0.52 ± 0.069	0.56 ± 0.17

Table 4: Renal Function Tests- Nephrotoxic cases

Parameter	Healthy dogs	Diseased dogs 1st day	Diseased dogs 7th day
Blood Urea Nitrogen (mg/dl)	16.29 ± 3.46	219.80 ± 55.12	285.00 ± 114.77
Creatinine (mg/dl)	0.33 ± 0.09	13.15 ± 2.87	19.51 ± 2.99
Urine Specific gravity	1.035	1.0129 ± 0.001	1.0150 ± 0.002
Urine Protein Creatinine ratio	0.38 ± 0.05^{a}	4.50 ± 0.54^{b}	3.83 ± 0.93^{b}
Urine N-Acetyl-β-Glucosaminidase (NAG) (U/g of creatinine)	7.08 ± 1.00^{a}	69.22 ± 31.93^{b}	
Urine γ-Glutamyl transferase (GGT) (IU/L/mmol creatinine)	1.02 ± 0.42^{a}	14.12 ± 9.16^{b}	
Urine Alkaline phosphatase (ALP) (IU/L/mmol creatinine)	5.78 ± 1.57^{a}	63.11 ± 32.40^{b}	

Means with different superscripts are significantly different(5% level)

Table 5:Serum Potassium and GGT- Nephrotoxic cases

Parameter	Healthy dogs	Diseased dogs 1st day	Diseased dogs 7th day
Serum Potassium mEq/L	4.1 ± 1.56	6.35 ± 1.86	6.11 ± 1.29
Serum GGT IU/L	6.25 ± 1.02	18.25 ± 7.62	25.75

Table 6: Haematology ,Serum biochemistry, Urinalysis and Urinary Enzyme

Studies of Mirofiraemic dogs (n=4)

Parameter	Healthy Controls	Diseased 1st day	Diseased 7th day
Haemoglobin (g%)	14.033 ± 0.80	10.15 ± 2.08	11.83 ± 2.47
Total erthrocyte count (mill/mm3)	7.017 ± 0.46	5.70 ± 0.89	5.57 ± 1.19
Volume of packed red cells (%)	38.13 ± 2.89	29.60 ± 6.55	34.06 ± 7.65
Erytrocyte sedimentation rate(mm/hr)	3.00 ± 0.37	61.50 ± 32.04	47.66 ± 41.28
Total leucocyte count(/mm3)	13900 ± 516.40	15925 ± 3699.40	20400 ± 5146.84
Neutrophils (%)	77.17 ± 1.94	74.75 ± 5.73	78.66 ± 2.90
Lymphocytes (%)	21.83 ± 4.58	18.50 ± 2.90	16.25 ± 2.05
Eosinophils(%)	1.00 ± 0.33	4.75 ± 3.11	3.00 ± 0.81
Platelet count(10^3/mm^3)	373 ± 38.95	297.0 ± 87.13	407.33 ± 137.78
Total Protein (g/dl)	5.85 ± 0.22	8.22 ± 0.24	8.36 ± 0.18
Albumin (g/dl)	2.16 ± 0.12	2.30 ± 0.10	1.94 ± 0.41
Globulin (g/dl)	3.69 ± 0.16	5.92 ± 0.30	6.41 ± 0.24
Albumin Globulin (AG) Ratio	0.60 ± 0.04	0.39 ± 0.02	0.31 ± 0.04
Serum Potassium mEq/L	4.1 ± 1.56	4.42 ± 0.37	4.35 ± 0.38
Serum GGT IU/L	6.25 ± 1.02	14.07 ± 2.69	9.00 ± 2.13
Kidney Function Tests			
Blood Urea Nitrogen (mg/dl)	16.29 ± 3.46	216.75 ± 79.97	173.74 ± 79.05
Creatinine (mg/dl)	0.33 ± 0.09	10.79 ± 2.72	8.43 ± 3.47
Urine Specific gravity	1.035 ± 0.001	1.0125 ± 0.002	1.0117 ± 0.001
Urine Protein Creatinine ratio	0.38 ± 0.05	4.44± 1.91	7.99 ± 2.60.
Urinary Enzymes		**Dog 1**	**Dog 2**
Urine N-Acetyl-β-Glucosaminidase (NAG) (U/g of creatinine)	7.08 ± 1.00 [a]	15.99 [b]	50.91 [b]
Urine γ-Glutamyl transferase (GGT) (IU/L/mmol creatinine)	1.02 ± 0.42 [a]	3.67 [b]	7.13 [b]
Urine Alkaline phosphatase (ALP) (IU/L/mmol creatinine)	5.78 ±1.57 [a]	54.29 [b]	44.25 [b]

Means with different superscripts are significantly different(5% level)

Table: 7 Haematology , Serum biochemistry, Urinalysis and Urinary Enzyme

Studies of dogs with pyometra(n=3)

Parameter	Healthy Controls	Diseased 1st day (Mean & range)	Diseased 7th day (Mean & range)
Haemoglobin (g%)	14.033 ± 0.80	7.67(4.8-10.5)	7.90(6.4-9.4)
Total erthrocyte count (mill/mm3)	7.017 ± 0.46	3.40(1.72-5.14)	3.65(2.9-4.4)
Volume of packed red cells (%)	38.13 ± 2.89	23.70(15.4-32.8)	24.40(19.5-29)
Erytrocyte sedimentation rate(mm/hr)	3.00 ± 0.37	74.50(15-134)	82.50(45-120).
Total leucocyte count(/mm3)	13900 ± 516.40	25433.33(9400-33800)	17650(11300-24000)
Neutrophils (%)	77.17 ± 1.94	72.33 (67-75)	69.5 %(65-74)
Lymphocytes (%)	21.83 ± 4.58	20.33 (20-21)	20.33(20-21)
Eosinophils(%)	1.00 ± 0.33	3.33 (1-5)	3.33(1-5)
Platelet count(10^3/mm^3)	373 ± 38.95	171(98-242)	201
Total Protein (g/dl)	5.85 ± 0.22	7.5g(6.8-8.7)	8.00
Albumin (g/dl)	2.16 ± 0.12	2.47(2.3-2.7)	2.00
Globulin (g/dl)	3.69 ± 0.16	5.03 (4.1 – 6.4)	6.00
Albumin Globulin (AG) Ratio	0.60 ± 0.04	0.53 (0.4-0.7)	0.33
Serum Potassium mEq/L	4.1 ± 1.56	5.7	6.6
Serum GGT IU/L	6.25 ± 1.02	9.0 (8-10)	8.67 (7-10)
Kidney Function Tests			
Blood Urea Nitrogen (mg/dl)	16.29 ± 3.46	133(78-190)	84.50(59-110)
Creatinine (mg/dl)	0.33 ± 0.09	10.90(6.1-15)	9.75(4.2-15.3).
Urine Specific gravity	1.035 ± 0.001	1.01.	1.01.
Urine Protein Creatinine ratio	0.38 ± 0.05	8.60(5.5-11.7)	
Urinary Enzymes		**Dog 1**	**Dog 2**
Urine N-Acetyl-β-Glucosaminidase (NAG) (U/g of creatinine)	7.08 ± 1.00 [a]	125.94 [b]	180.72 [b]
Urine γ-Glutamyl transferase (GGT) (IU/L/mmol creatinine)	1.02 ± 0.42 [a]	32.39 [b]	82.48 [b]
Urine Alkaline phosphatase (ALP) (IU/L/mmol creatinine)	5.78 ±1.57 [a]	30 [b]	324.66 [b]

Means with different superscripts are significantly different(5% level)

Table:8 Haematology, Serum biochemistry, Urinalysis and Urinary Enzyme Studies of dogs with enlargement of Prostate (n=3)

Parameter	Healthy Controls	Diseased 1st day (Mean & range)	Diseased 7th day (Mean & range)
Haemoglobin (g%)	14.033 ± 0.80	11.07 (6.9-14.5)	9.00 (3.00-15.4)
Total erthrocyte count (mill/mm3)	7.017 ± 0.46	6.39(6.38-6.4)	6.47(6.2-6.74)
Volume of packed red cells (%)	38.13 ± 2.89	43.25(41.5-45)	37.10 (33 – 41.2)
Erytrocyte sedimentation rate(mm/hr)	3.00 ± 0.37	28.5(2-55)	41.5 (3-80)
Total leucocyte count(/mm3)	13900 ± 516.40	20025.00(12700-27350)	32450 (32300-32600)
Neutrophils (%)	77.17 ± 1.94	76.50 (76-77)	79 (79-79)
Lymphocytes (%)	21.83 ± 4.58	21.50 (21-22)	19
Eosinophils(%)	1.00 ± 0.33	2	2
Platelet count(10^3/mm^3)	373 ± 38.95	180.66(152-198)	193(180-206)
Total Protein (g/dl)	5.85 ± 0.22	7.87(6.5-8.87)	7.5 (6.8-8.2)
Albumin (g/dl)	2.16 ± 0.12	2.31 (2.1-2.7)	2.35(2.00-2.70)
Globulin (g/dl)	3.69 ± 0.16	4.98 (3.8-6.15)	5.15 (4.1-6.2)
Albumin Globulin (AG) Ratio	0.60 ± 0.04	0.52 (0.34-0.7)	0.51(0.32-0.7)
Serum Potassium mEq/L	4.1 ± 1.56	4.45(4.3-4.6)	4.55 (4.3-4.8)
Serum GGT IU/L	6.25 ± 1.02	11.75 (5.5-18)	17.57 (11-24)
Kidney Function Tests			
Blood Urea Nitrogen (mg/dl)	16.29 ± 3.46	162.33 (120-216)	241.90 (191-292.80)
Creatinine (mg/dl)	0.33 ± 0.09	16.33 (11.00-18.80)	16.08(11.06-21.1)
Urine Specific gravity	1.035 ± 0.001	1.01	1.01
Urine Protein Creatinine ratio	0.38 ± 0.05	3.57 (2.6-4.53)	
Urinary Enzymes		**Dog 1**	**Dog 2**
Urine N-Acetyl-β-Glucosaminidase (NAG) (U/g of creatinine)	7.08 ± 1.00 [a]	456.44 [b]	21.14 [b]
Urine γ-Glutamyl transferase (GGT) (IU/L/mmol creatinine)	1.02 ± 0.42 [a]	34.12 [b]	2.01 [b]
Urine Alkaline phosphatase (ALP) (IU/L/mmol creatinine)	5.78 ±1.57v	17.14 [b]	10.71 [b]

Means with different superscripts are significantly different(5% level)

Table: 9 Haematology, Serum biochemistry, Urinalysis and Urinary Enzyme Studies of dogs with Pancreatitis (n=2)

Parameter	Healthy Controls	First day		Seventh day	
		Dog 1	Dog 2	Dog 1	Dog 2
Haemoglobin (g%)	14.033 ± 0.80	6.00	5.1	6.1	4.8
Total erthrocyte count (mill/mm3)	7.017 ± 0.46	3.06	2.8	3.38	2.1
Volume of packed red cells (%)	38.13 ± 2.89	17.2	17	19.4	18
Erytrocyte sedimentation rate(mm/hr)	3.00 ± 0.37	5	36	3	40
Total leucocyte count(/mm3)	13900 ± 516.40	13300	8700	16100	6500
Neutrophils (%)	77.17 ± 1.94	75	69	88	72
Lymphocytes (%)	21.83 ± 4.58	20	23	11	26
Eosinophils(%)	1.00 ± 0.33	3	7	1	2
Platelet count(10^3/mm^3)	373 ± 38.95	245	318	259	305
Total Protein (g/dl)	5.85 ± 0.22	6.2	5.12	5.8	6.42
Albumin (g/dl)	2.16 ± 0.12	2.4	1.53	2.2	1.88
Globulin (g/dl)	3.69 ± 0.16	3.8	3.59	3.6	4.54
Albumin Globulin (AG) Ratio	0.60 ± 0.04	0.6	0.42	0.6	0.41
Serum Potassium mEq/L	4.1 ± 1.56	8.54	4.61	8.5	6.41
Serum GGT IU/L	6.25 ± 1.02	7.8	11	8.1	9
Kidney Function Tests					
Blood Urea Nitrogen (mg/dl)	16.29 ± 3.46	154	190	132	165
Creatinine (mg/dl)	0.33 ± 0.09	18	26	14.3	18.94
Urine Specific gravity	1.035 ± 0.001	1.01	1.015		1.015
Urine Protein Creatinine ratio	0.38 ± 0.05	9.94	2.1		2
Urinary Enzymes					
Urine N-Acetyl-β-Glucosaminidase (NAG) (U/g of creatinine)	7.08 ± 1.00 [a]	28.21 [b]			
Urine γ-Glutamyl transferase (GGT) (IU/L/mmol creatinine)	1.02 ± 0.42 [a]	18.55 [b]			
Urine Alkaline phosphatase (ALP) (IU/L/mmol creatinine)	5.78 ±1.57 [a]	113.48 [b]			

Means with different superscripts are significantly different(5% level)

Table 10: Haematology, Serum biochemistry, Urinalysis and Urinary Enzyme Studies of dogs with rhabdomyolysis and Leptospirosis

Parameter	Healthy Controls	Rhabdomyolysis		Leptospirosis	
		Day 1	Day 7	Day 1	Day 7
Haemoglobin (g%)	14.033 ± 0.80	17		10.3	10.2
Total erthrocyte count (mill/mm3)	7.017 ± 0.46	6.87		6.23	6.6
Volume of packed red cells (%)	38.13 ± 2.89	56.8		32.6	31
Erytrocyte sedimentation rate(mm/hr)	3.00 ± 0.37	2		10	26
Total leucocyte count(/mm3)	13900 ± 516.40	38600		64600	72400
Neutrophils (%)	77.17 ± 1.94	68		80	82
Lymphocytes (%)	21.83 ± 4.58	28		15	15
Eosinophils(%)	1.00 ± 0.33	2		1	2
Platelet count(10^3/mm^3)	373 ± 38.95	260		128	242
Total Protein (g/dl)	5.85 ± 0.22	5.6		5.3	4.27
Albumin (g/dl)	2.16 ± 0.12	2.7		2.3	1.59
Globulin (g/dl)	3.69 ± 0.16	2.9		3	2.68
Albumin Globulin (AG) Ratio	0.60 ± 0.04	0.7		0.76	0.59
Serum Potassium mEq/L	4.1 ± 1.56	5		6.4	6.8
Serum GGT IU/L	6.25 ± 1.02	38		8.2	9.34
Kidney Function Tests					
Blood Urea Nitrogen (mg/dl)	16.29 ± 3.46	123		256	372
Creatinine (mg/dl)	0.33 ± 0.09	5.6		11.23	18
Urine Specific gravity	1.035 ± 0.001	1.007		1.010	1.015
Urine Protein Creatinine ratio	0.38 ± 0.05			13.54	
Urinary Enzymes					
Urine N-Acetyl-β-Glucosaminidase (NAG) (U/g of creatinine)	7.08 ± 1.00 [a]			124.16 [b]	
Urine γ-Glutamyl transferase (GGT) (IU/L/mmol creatinine)	1.02 ± 0.42 [a]			4.49 [b]	
Urine Alkaline phosphatase (ALP) (IU/L/mmol creatinine)	5.78 ±1.57 [a]			42.62 [b]	

Means with different superscripts are significantly different(5% level)

Table.11: Effect of Peritoneal dialysis on azotaemia in renal failure

Dog No	Predialysis Data		Post Dialysis data	
	BUN mg/dl	Creatinine mg/dl	BUN mg/dl	Creatinine mg/dl
1	182	25.2	168	23.1
2	516	27.4	420	24.3
3	195	15.2	108	11.3
4	372	18	264	13.1
5	131	11.6	discontinued	
6	279	17.8	236	15.8

Discussion

5. DISCUSSION

Renal disease implies a pathological or functional lesion of any size, distribution, cause or degree of functional impairment in one or both kidneys. It may be subclinical due to large renal reserve. Renal failure refers to the clinical syndrome that occurs when the kidneys are no longer able to maintain their regulatory, excretory and endocrine functions, resulting in retention of nitrogenous solutes and derangements of fluids, electrolytes and acid base balance. Acute uraemia is a clinical condition in which the kidneys suddenly fail to meet the excretory, metabolic and endocrine demands of the body .Chronic renal failure is defined as a primary kidney disease that has persisted for months to years and is characterized by a progressive destruction of nephrons (DiBartola, 2005).

Dogs presented to the University Veterinary Hospital, Kokkalai and Veterinary College hospital, Mannuthy with clinical signs suggestive of renal failure/disease with serum creatinine value above normal range (IRIS, 2006) were selected for this study. Creatinine level was increased in both acute and chronic renal failure, irrespective of the cause, but the two conditions could not be differentiated as the cases were presented at the hospital in its end stages.

5.1 SIGNALMENT:

Twenty three cases were selected for the study of which 65 % were males. Antony (2004) while reporting on urinary tract disorders in dogs found that 63% of affected dogs were males. Eubig *et al.* (2005) reported that among dogs with acute renal failure after the ingestion of grapes or raisins 62.8% were males which are in conformity with the findings of this study. Vaden *et al.*(1997) concluded from a retrospective study of acute renal failure that intact male dogs were more likely to develop ARF. The present finding agrees with it. Birnbaum *et al.* (1998) reported that among the dogs affected with acute renal

failure due to leptospirosis, 53 % were males and opined that there was no sex predisposition in dogs naturally infected with leptospirosis.

The reason for the increased representation of male dogs might be the demographic pattern of dogs which was biased towards males. According to the "*17th Quinquennial Livestock Census in Kerala*". (Government of Kerala, 2004) 81.31% of the dogs of Kerala state and 75.33% of Trichur district were males.

German shepherd dogs were found to be the most susceptible breed to renal failure with an occurrence of 35%. This is in agreement with Antony (2004) who reported an incidence of 44% of urinary tract disorders in German shepherd dogs.

Age of affected animals ranged from 4 months to 13 years and the most susceptible age group was found to be 4-8 years and this might be due to the fact that majority of dogs presented to the hospital were of this age group. Another factor might be the reduced renal function of dogs over five years of age as reported by Leibetseder and Neufield (1991).

In young animals renal disease is often thought to be congenital because of the lack of long term signs, however development of lesions consistent with an end stage kidney may develop in as little as 60 days. (Finco, 1995).

Birnbaum *et al.* (1998) reported that the median age of dogs affected with acute renal failure due to leptospirosis was 7.4 years with range of 2 months to 13 years which agrees with the current finding.

Majority of the animals were vaccinated against rabies and other major infectious diseases which indicated that the diseased animals were cared well by their owners. Immune mediated hemolytic anaemia, immune mediated thrombocytopaenia, icterus, polyarthritis, renal failure and glomerulonephritis

had been listed as possible vaccine related complications in canine vaccine guidelines. (AAHA, 2006). Greene and Schultz (2005) opined that glomerulonephritis and amyloidosis could result from chronic or repeated antigenic exposure.

As per the present study, the important causes of renal failure in descending order were exposure to nephrotoxic drugs, microfilaraemia, pyometra, enlargement of prostate gland and pancreatitis. Rhabdomyolysis and leptospirosis were also noticed. The important clinical signs observed were lethargy, anorexia, vomiting, melena, anuria or oliguria, muscle weakness, polyuria, oral ulcers, jaundice, ascites, oedema, exercise intolerance and haemoglobinuria.

Based on etiology, 23 cases of renal failure were grouped, viz; renal failure as a result of exposure to nephrotoxic drugs (n=9), renal failure associated with microfilaraemia (n=4),. Pyometra (n=3), enlargement of prostate gland (n=3), pancreatitis (n=2), rhabdomyolysis (n=1) and leptospirosis (n=1).

5.2 RENAL FAILURE ASSOCIATED WITH EXPOSURE TO NEPHROTOXIC DRUGS.

The history revealed that nine dogs which developed renal failure had exposure to nephrotoxic drugs in the recent past. Major factors influencing the development of drug induced nephrotoxicity are the dosage, duration of treatment and hydration status of the animal. Administration of excessive dosages, prolonged or repeated administration of nephrotoxic drugs or concurrent administration of other nephrotoxic drugs such as oxytetracycline and NSAIDS may substantially increase the risk of nephrotoxicity. Combination of nephrotoxic drugs even in minimal amounts may promote nephrotoxicity in hypovolaemic or dehydrated animals. Non nephrotoxic drugs such as diuretics might also enhance renal injury when administered with a nephrotoxic drug (Forrester *et al.*, 1994)

Oxytetracycline, meloxicam, gentamicin, and ceftriaxone were the nephrotoxic agents associated with renal failure in this study. These drugs were used either as combinations or as single drug.

Cowgill and Francey (2005) listed out the substances causing nephrotoxicity which included aminoglycosides, cephalosporins, tetracyclines and nonsteroidal antiinflammatory drugs.

All aminoglycosides could cause renal toxicity to some degree. They bind to the brush border of proximal tubular cells, accumulate in lysosomes, and inhibit lysosomal phospholipase. Toxicity was correlated with the degree of tubular reabsorption of the drug and inhibition of phospholipid metabolism in proximal tubules. Therefore gentamicin which exhibit the greatest degree of reabsorption and most potently interfere with phospholipid metabolism had the greatest potential to cause nephrotoxicity (Maddison and Watson, 2002)

Oxytetracycline might become toxic even in normal doses because it depended on renal excretion for its elimination. So according to Forrester and Little (1994) in subclinical renal disease excretion of oxytetracycline was reduced and its serum half-life increased resulting in toxicity.

Maddison and Johnston (2002) opined that synthesis of renal prostaglandins was inhibited by NSAIDs which were involved in maintaining renal blood flow via their vasodilatory actions. In a healthy well hydrated animal reduced renal prostaglandin production was of little consequence. However, significant renal toxicity could result if an animal was volume depleted, was avidly retaining sodium as in congestive heart failure or hepatic cirrhosis, or had preexisting renal insufficiency. NSAIDs like meloxicam and carpofen might cause toxicity if the animal is dehydrated or in a state of subclinical renal disease.

5.2.1 Signalment

In this study dogs in the age group of 5-10 years were more affected with renal failure following administration of nephrotoxic substances. Majority of clinical cases attended in the hospital belong to this age group and hence no special significance need be attached to this finding. The age range of 4 months to 13 years had been reported earlier by Eubig *et al.* (2005) while studying cases of renal failure following ingestion of raisins or grapes. They also found that male dogs were more affected which agree to the present finding. Morrow *et al.* (2005) also found the same age group as the most susceptible while studying renal toxicity of raisins.

5.2.2 Clinical observations

Vomiting, anorexia, lethargy, oliguria, polyuria, ataxia and weakness seen in the present study were similar to the observations made by Eubig *et al.* (2005) in raisin induced nephrotoxicity.

Uraemic animals were typically hypothermic and this might be related to the degree or severity of azotaemia (Cowgill and Francey, 2005). Visible mucous membranes were usually pink in dogs with acute renal failure (Cowgill and Francey, 2005). But it was pale in six, pink in two and congested in one dog in this study. This variation could be due to the difference in overall health status of affected dogs or concurrent infections.

The signs of acute uraemia included listlessness, depression, anorexia, vomiting, diarrhea and weakness as per Cowgill and Francey (2005). These were similar to the observations made in the current work. Lethargy and anorexia were noticed in all dogs, vomiting in 90 % of dogs, oliguria or anuria in 80 % of dogs, 70 % had melena , 60% had muscle weakness , 20% had oral ulcers and ascites and 10 % had haemoglobinuria, jaundice, oedema or

exercise intolerance . Vomiting in dogs with renal failure was not associated with food intake and they vomited 2-3 times daily (Muraly, 2001).

According to Fleming et *al.* (1989) oliguria or anuria was a cardinal sign of acute renal failure. Dehydration, anorexia, hypothermia and mucosal injection were the other signs listed.

In acute renal disease, the onset of signs was abrupt and the signs included anorexia, depression, vomiting and thirst. The rectal temperature was often normal, but an arched back, stiff gait, pain in the lumbar region, and full pulse could be encountered (Doxey,1983).

5.2.3 Clinical pathology

Haemogram

The median haematocrit value reported by Eubig *et al.* (2005) was 31% which conform to the present finding. There was an evident reduction in haemoglobin concentration, erythrocyte count and PCV when compared to normal animals which indicated the anaemic status of the dogs with renal disease.

The complete blood count in ARF might reveal anaemia or a normal haematocrit and leucocytosis (Kraje, 2002). The mild anaemia observed in the present study could be caused by gastrointestinal haemorrhage.

Haematological findings in a case of acute renal failure following snake bite was characterised by leukocytosis with shift to left, thrombocytopenia and prolonged coagulation times (Puig *et al.*, 1995).

Leucogram and Platelet Count

Results of the present study revealed mild leucocytosis and thrombocytopaenia when compared to the values recorded for normal dogs. The most important change in leucogram was the leucocytosis. Kraje (2002) also

opined that depending on the cause of renal failure there could be leucocytosis with shift to left.

Serum biochemical analysis:

Total Protein, Albumin, Globulin and A: G ratio:

The present findings were mean total protein, albumin, globulin and A: G ratio of 7.01± 0.29 g/dl, 2.35± 0.25g/dl, 4.66± 0.27g/dl and 0.52± 0.06 respectively on the day of admission. There was increase in total protein and reduction in A: G ratio compared to the healthy dogs. This may be due to the effect of renal failure on liver resulting in excessive globulin production. As a consequence, there was relative increase of globulin and total protein and decrease in A: G ratio. Similar observations were made by Muraly (2001), Eubig *et al.* (2005) and Mrudula *et al.* (2005)

Serum Creatinine

Plasma creatinine was increased in renal failure, whatever might be the cause, and correlated well with a decrease in GFR according to a curvilinear relationship, such that P-creatinine was insensitive for detecting moderate decreases of GFR or for monitoring progression of GFR in dogs with severely reduced kidney function (Braun *et al.,* 2003). Hence measurement of creatinine might not reflect early stage of renal disease. The mean serum creatinine in this group was 13.15± 2.87 mg/dl on the first day and 19.51± 2.99 mg/dl on 7^{th} day. The values were much higher than that of normal dogs and indicated the severity of azotaemia.

According to Cowgill and Francey (2005) renal dysfunction could be staged as mild in animals with a serum creatinine concentration of < 2.5 mg/dl (more than 40% normal function), moderate for those with a serum creatinine

concentration between 2.5 mg/dl and 5 mg/dl (between 40% and 20% of normal function), severe for those with a serum creatinine concentration between 5 mg/dl and 10 mg/dl (between 20% and 10 % of normal function) and extreme if the serum creatinine concentration is greater than 10 mg/dl (<10% of normal function). All the dogs included in this group were in the extreme renal dysfunction category and that could be the reason for the treatment failure. Similar findings were recorded by Gopegui *et al.* (1999) in a dog with iatrogenic bilateral hydroureter and hydronephrosis and Puig *et al.* (1995), in a dog with renal failure after snake bite.

Blood Urea Nitrogen:

Blood urea nitrogen level observed on the day of admission was 219.80 ± 55.12 mg/dl as against normal value of 16.29 ± 3.46 mg/dl. Blood urea nitrogen increased inversely with reductions in glomerular filtration rate and contributed to the developing azotaemia. It was influenced by numerous extra renal parameters that made its concentration less specific as a marker of renal function (Cowgill and Francey, 2005). Mrudula *et al.* (2005) also observed increased BUN values (263.94 ± 18.92mg/dl) in dogs with nephritis while Langston (2002) reported acute renal failure in four cats following ingestion of Easter lily in which the concentration of blood urea nitrogen were 165 mg/dl,240 mg/dl,265 mg/kg and 158 mg/dl.

Medaille *et al.* (2004) evaluated the relationship between serum/plasma urea and serum/plasma creatinine and found that in 27.55% of the cases urea concentration was increased while creatinine was normal. In 1.6% of cases creatinine concentration showed higher values while urea was normal. The authors opined that this discrepancy might be due to non renal factors and variation in muscle mass of the animals. Estimation of serum creatinine level is considered a better indicator of renal function.

Serum GGT

The mean serum GGT value among dogs with renal failure in this study was 18.25 ± 7.62 IU/L which was slightly above the reference value of 0-10 IU/L. The multisystem involvement of renal failure could affect the hepatic function.

Ward (1976) did not observe such rise in plasma γ GT activity either in the first three hours or at any time in eight days following the ischaemic period in experimentally induced renal ischaemia.

Potassium

Mean serum potassium level in dogs with renal failure following exposure to nephrotoxic drugs was found to be 6.35 ± 1.86 mEq/ L on the first day. Renal failure produced hyperkalaemia only when the glomerular filtration rate was severely compromised, producing either an oliguric or anuric state according to Rubin and LeClerc (2001). Majority (7/9) of the dogs in this group were in an oliguric or anuric state.

Worwag and Langston (2008) also observed potassium value of 6.45 ± 1.2 mEq/L in cats with acute renal failure. The author also reported that for each unit increase of potassium there was a 57 % decrease in the chances of survival.

Urinalysis

Qualitative analysis

The mean specific gravity was 1.0129± 0.001 on the first day. Benjamin (1985) stated that the normal urine specific gravity in dogs was in the range of 1.015-1.045 with an average of 1.025 in dogs. All the dogs in the present study were showing isosthenuric or hyposthenuric range of specific gravity. In end stage renal disease the specific gravity was usually from 1.003-

1.015 due to the inability of kidneys to concentrate urine. The closer the specific gravity to 1.010 the lesser the functioning of kidney tissue. Acute renal failure could give exactly the same results as chronic renal failure.

McCaw *et al.* (1989b) stated that the glomerular filtrate has a specific gravity of 1.007 to 1.015. Urine with a specific gravity outside this isosthenuric range had been altered by kidney tubules which require functional hypothalamic osmoreceptors, production and release or inhibition of anti diuretic hormone and a renal medulla of sufficient hypertonicity or in other words a sufficiently functional kidney.

Kraje (2002) and Eubig *et al.* (2005) also observed specific gravity of 1.030 and $\leq$ 1.029 in dogs with renal failure.

Puig *et al.* (1995) reported urine specific gravity of 1.021 in a dog with acute intrinsic renal failure following snakebite in a dog. Fleming et al. (1989) reported that renal parenchymal disease was associated with a urine specific gravity of 1.010-1.017 which was in agreement with the present finding.

Presence of protein in urine was qualitatively examined and an average of 3+ was noticed. Normal random urine samples contain between 0 and 50 mg/dl of protein. The presence of protein in urine is more significant when urine specific gravity is low (Mikiciuk *et al.,* 1989). Proteinuria with low specific gravity of urine found in the present study indicated severe renal damage.

Quantitative analysis

The mean value of urine protein creatinine ratio was 4.50 ± 0.54 on the day of admission. According to Mikiciuk *et al.* (1989) if the value of urine protein creatinine ratio was greater than 2, the dog was losing an abnormal amount of protein. A UPC value of 5-7 indicated that daily urine protein loss is between 110-150 mg/Kg bodyweight.

N-Acetyl-β-D-Glucosaminidase (NAG)

N-Acetyl-β-D-Glucosaminidase, a lysosomal enzyme which is found predominantly in proximal tubules and increased activity of this enzyme in urine indicated tubular injury. N-Acetyl-β-D-Glucosaminidase index was found to be increased after exposure to various toxic substances such as lead and cadmium, solvents, contrast media, aminoglycosides, other nephrotoxic drugs and various human glomerular diseases including diabetic nephropathy (Ebisawa *et al.*, 2006). The mean NAG value was 69.22 ± 31.93 U/g of creatinine in nephrotoxic group whereas in healthy animals it was 7.08 ± 1.00 U/g of creatinine. The difference in values are statistically significant ($P<0.05$). Uechi *et al.* (1994) also observed NAG index of 5.7 ± 3.4 U/g of creatinine in normal healthy dogs whereas Reusch *et al.* (1991) , Sato *et al.* (2002) and Brunker *et al.* (2009) observed slightly lower values of NAG index in normal dogs and this variation might be due to variations in the procedure adapted. In the present study ρ-nitrophenyl N-Acetyl-β-D-Glucosaminide was used as the substrate and the same was used by Sato *et al.* (2002) who observed NAG index values ranging between 15.7 and 136.8 U/g of creatinine in dogs with renal failure. Reusch *et al.* (1991) used 3-cresolsulphonephtaleinyl N -Acetyl-β-D-Glucosaminide and Uechi *et al.*(1994) used sodio-meresolsulphonephtaleinyl N- acetyl - β-D-Glucosaminide as substrate.

γ Glutamyl transpeptidase (GGT)

γ Glutamyl transpeptidase and alkaline phosphatase are renal tubular brush border enzymes found in low concentrations in normal urine and much higher levels in renal tubular injury. The cells of the kidney most sensitive to ischaemic injury are those of the proximal convoluted tubules and the first detectable change in the architecture of these cells following ischaemia is the loss of their brush border. The highest activity of GGT could be detected in the kidneys among the various mammalian tissues (Ward,1976). Hence any tubular insult or injury could be detected by estimation of GGT activity in urine.

Urinary GGT activity rose dramatically (78 fold increase) after 90 minute complete renal ischaemia from a mean of 112m Units in 15 minutes to a peak of 8727 m Units as reported by Ward (1976). The author suggested GGT as a sensitive indicator to assess renal tubular injury provided that there was adequate urine flow and that the renal insult was not too severe.

The mean value of urinary GGT was 1.02 ± 0.42 IU/m mol of creatinine in healthy dogs. Brunker *et al.* (2009) observed that the mean urinary GGT value in normal dogs was 13.49 ± 7.03 U/g of creatinine and the reference range proposed by them was 1.93 - 28.57 U/g of creatinine. In the present study it was 14.12 ± 9.16 IU/m mol of creatinine.

Heiene *et al.* (2001) classified experimental dogs on the basis of urinary GGT and ALP as low (<10IU/m mol of creatinine), Intermediate (10-20) and high (>20) and found that high urinary enzyme values were associated with severe histopathological lesions in the proximal tubular cells and reduced GFR.

Heiene *et al.* (1991) found that the median values for urinary GGT was 3.4 IU/L/m mol of creatinine in normal dogs , 4.9 IU/L/m mol of creatinine in CRF and 9.6 IU/L/m mol of creatinine in ARF. The authors opined that urinary GGT was less useful as a marker of acute renal damage and could not found any clear correlations between the enzyme levels and extent of morphological kidney damage. The variation could be due to the fact that there was a within day variation in GGT excretion and even in dogs with proven renal damage the GGT levels varied within the day between normal and high. At a later stage however all dogs had high GGT levels (Gosset *et al.*, 1987).

Alkaline Phosphatase (ALP)

Alkaline phosphatase was a sensitive indicator for assessing acute tubular dysfunction.

The mean values of ALP was 5.78 ±1.57 IU/mmol creatinine in healthy dogs. In the diseased group it was 63.11 ± 32.40 IU/mmol of creatinine.

Heiene *et al.* (1991) also observed similar results in healthy and diseased dogs and according to them urinary ALP was a better marker than urinary GGT.

5.2.4 Ultrasonography

Hyperechoic kidneys with no corticomedullary distinction were the most common observation on ultrasonography. It was seen in seven dogs in this group. One dog had hypoechoic kidneys with reduced corticomedullary distinction. In one dog kidney showed normal echotexture. Liver with focal hyperechoic areas were seen in two dogs. Thinning of cortical area was noticed in one dog, prostate was slightly enlarged and hyperechoic and bladder with urine containing hyperechoic particles in one dog.

Hyperechoic kidneys were associated with diffuse infiltrative diseases. Widmer *et al.* (2004) opined that many infiltrative processes of the renal parenchyma resulted in fibrosis and replacement of functional tissue and therefore could be ultrasonographically similar. Because of the tremendous reserve capacity of the kidney, renal echogenicity could not be related to function. Authors also pointed out that kidneys with end stage disease were often diffusely hyperechoic and have poor corticomedullary delineation and an irregular shape. In addition many kidneys with end stage disease were small and had decreased cortical thickness and irregular margination with thick capsules.

Diffusely hypoechoic kidneys were seen less frequently than hyperechoic kidneys. Lymphoma is an infiltrative process that may be expected to cause a generalized decrease in renal echogenicity because it is associated with a hypoechoic change in other solid organs. Almost all conditions that caused renal oedema reduced echogenicity (Widmer *et al.*, 2004)

Diffuse increase in echogenicity could be associated with nephritis, acute tubular necrosis, nephrocalcinosis, hypercalcaemic nephropathy and end stage kidney disease (Lamb, 1990).

Triolo and Miles (1995) reported that bilateral increase in renal size could occur in abnormalities like acute nephritis, polycystic kidney, lymphosarcoma, perirenal pseudocyst, hydronephrosis or pyelonephritis.

5.2.5 Treatment and response to treatment

Renal failure is a serious disease and affected patients have a guarded prognosis. All the animals were treated with specific therapeutic aims to correct fluid imbalances and electrolyte derangements, provision of adequate nutrition and symptomatic supportive care to control ulceration and vomiting.

None of the animals responded favourably to routine therapy with fluids, diuretics, antibiotics and other symptomatic therapy. One of the animals died on the same day of admission, one on the second day, and one on fifth day. Only one animal survived for more than one month which also died before completing two months. The reason for this failure of treatment could be the fact that all the animals were presented to the hospital in the later stages of disease.

Peritoneal dialysis

Six animals which were not responding to routine therapy were subjected to peritoneal dialysis. It was discontinued in one animal following complications of haemorrhage and non return of peritoneal dialysis fluid. The

pre and post dialysis data of serum creatinine and BUN indicated that there was a reduction in azotaemia in all cases even though not statistically significant.

Dialysis improves azotaemia, electrolyte disturbances, acid base status and fluid balance allowing time for kidney function to improve. The main complications of peritoneal dialysis were hypoalbuminaemia, catheter occlusion or exit site leaks and peritonitis. The equipment necessary for peritoneal dialysis was readily available. It could be an excellent treatment modality when performed by a motivated and conscientious veterinary team, but it was a laborious and methodologically rigorous process that should not be undertaken blithely. (Langston, 2003).

Dorval and Boysen (2007) tried peritoneal dialysis for the treatment of ARF in six cats and found that it was an effective renal replacement therapy for ARF in cats and carries a reasonable prognosis in selected cases. Complications noticed included subcutaneous oedema, hyperglycaemia, dialysate retention and hypoalbuminaemia.

Peritoneal dialysis was an effective option in the case of acute renal failure due to canine babesiosis. However it was insufficient when renal azotaemia was accompanied by other disease syndromes related to oxygen deficiency in tissues and hematological changes (Pomianowski *et al.*,2008).

In the present trial peritoneal dialysis was tried as a last resort in animals with end stage renal disease. A maximum of five fluid replacements could only be done in each case and the catheter was removed afterwards. Delay in fluid retrieval was the most important complication noticed. The results of the present trial indicated that further studies on the effectiveness of peritoneal dialysis were required.

5.2.6 Postmortem and Histopathological examination:

The postmortem lesions were suggestive of end stage renal failure. Severe gastrointestinal involvement, compensatory enlargement of heart and oedema of lungs were seen.

Minkus *et al.* (1994) observed that the main cause of primary renal azotaemia in dogs and cats were chronic interstitial nephritis of medium or high grade severity. Overall 70.4% of azotaemic cats and 58.3% azotaemic dogs showed chronic interstitial inflammation. The frequency of glomerulonephritis in its various forms was lower than that of chronic tubulo interstitial nephritis. Animals with chronic tubulointerstitial nephritis were considerably older (8.6 years) than animals with glomerulonephritis (5.3 years).

5.3 RENAL FAILURE ASSOCIATED WITH MICROFILARAEMIA

Wet film examination of four dogs with renal failure showed moderate to severe microfilaraemia. No other evident cause for renal failure was detected in these cases. The chronic parasitaemia may be the inciting cause for the lesion. Velthuysen and Florquin (2000) observed glomerular lesions in parasitic infections. Most of these lesions were proliferative and therefore showed an accumulation of cells in the glomerular tuft, either membranoproliferative or mesangioproliferative type of glomerulonephritis. There was a clear association between filariasis and glomerular disease as suggested by Winter and Majid (1984) and Velthuysen and Florquin (2000).

5.3.1 Signalment:

All affected animals were males and of comparatively younger age group with an average age of 6.5 years. The observation by Minkus *et al.* (1994) that dogs affected by glomerulonephritis were of a younger age group and that of Velthuysen and Florquin (2000) that microfilaraemia caused glomerulonephritis agreed with the present study.

5.3.2 Clinical Observations

The mean temperature, pulse and respiration rates of microflaraemic dogs were 101.3°F, 89.75/min and 21/min respectively. Two animals showed hind limb weakness, one dog had conjunctivitis and another had skin lesions. Lethargy, vomiting and anorexia were seen in all the dogs, polyuria and muscular weakness in two and oliguria and oral ulcers in one dog each.

Grauer (2005) Opined that the clinical signs associated with mild to moderate urinary protein loss were usually nonspecific and included weight loss and lethargy. But if the disease process progressed to a stage where more than three quarters of the nephrons were lost renal failure and resultant azotaemia, polydipsia, polyuria, anorexia, nausea and vomiting occurred and the presented cases in this group seemed to be in such a stage.

5.3.3 Clinical pathology

Haemogram:

The relevant observations in haemogram were reduced haemoglobin percentage, reduced erythrocyte count and PCV which indicated anaemia. A non regenerative anaemia was expected in this case as stated by Benjamin (1985) and McCaw *et al.* (1989b). Anaemia might be due to haemolysis as a result of destructive motility of microfilariae as suggested by Kitagava *et al.* (1989) or by decreased production of erythropoietin by the damaged kidney (Benjamin,1985)

Mrudula *et al.*(2005) while examining 60 nephritis cases found that the mean PCV % was 25.3±1.09, mean haemoglobin 7.67 ± 0.35 g %, total erythrocyte count 3.75 ± 0.16 mill/mm^3 and total leukocyte count 22.29± 1.86thou/ mm^3 which is similar to the present finding.

Leucogram and platelet count

The mean leucogram on first day did not have any specific variation whereas on the seventh day mild leucocytosis with neutrophilia, lymphopaenia and eosinopaenia were seen which indicated a stress leucogram as suggested by Benjamin(1985). Platelet count was within normal limits.

Serum Biochemical Analysis

Total protein, Albumin, Globulin and AG ratio

Hyperproteinaemia, hyperglobulinaemia and reduced AG ratio were the salient features of protein profile.The hyperproteinaemia might be due to the increased production of globulins in response to the continued presence of microfilarial antigen in blood.

Serum creatinine

The mean serum creatinine level on the day of admission was 10.79 ± 2.72mg/dl while that of seventh day was 8.43 ± 3.47 mg/dl. Mrudula *et al.* (2005) recorded a similar finding while examining the serum biochemical values of dogs with nephritis.

The international renal interest society (2006) had proposed a staging of chronic kidney disease based on plasma creatinine concentration. According to it four stages had been identified.

Stage 1 with serum creatinine less than 1.4mg/dl which is nonazotaemic, but with some other renal abnormality present like inadequate concentrating ability without identifiable non renal cause. Stage 2 with serum creatinine value 1.4-2.0 mg/dl had mild renal azotaemia, with mild or no clinical signs. But animals with creatinine value close to the upper limit of normal often had excretory failure.

Stage 3 with serum creatinine 2.1-5.0 mg/dl described as moderate renal azotaemia and in such cases many moderate clinical signs could be present.

Stage 4 with serum creatinine values more than 5.00mg/dl with severe renal azotaemia and many extra renal clinical signs would be present.

The mean creatinine level in this group indicated that all the animals considered for this study was in the 4th stage where there was severe azotaemia and multi system failure had been initiated.

Blood urea Nitrogen

Mean blood urea nitrogen level of affected dogs on first day was 216.75 ± 79.97 mg/dl while that of seventh day was 173.74 ± 79.05 mg/dl. The increase in blood urea nitrogen might be due to the severe kidney damage resulted from the prolonged presence of microfilarial antigen and the intravascular haemolysis as opined by Kitagava *et al.* (1989) and Langharnrner *et al.*(1997)

Increased blood urea nitrogen shown by the dogs in this group was similar to the finding reported by Benjamin (1985), Mridula *et al.* (2005) and Raila *et al.* (2007).

Serum GGT:

Serum GGT on day of presentation was 14.07 ± 2.69 IU/L while that of seventh day was 9.00 ± 2.13 IU/L. The slight increase in the serum GGT value might be the result of liver damage which occurred due to the multisystem involvement of renal failure as reported by Benjamin (1985) or due to the presence of large number of microfilariae in hepatic vessels.

Serum Potassium

Serum potassium was in the normal level in the present study which according to Polzin *et al.* (2005) was a normal phenomenon. The authors also said that even though there was an association between hypokalaemia and chronic kidney disease in cats, it was uncommon in untreated dogs in which species, hypokalaemia occur primarily as an iatrogenic complication of fluid therapy.

Urinalysis

Presence of protein in urine was at 2+ levels and urine specific gravity was 1.0125 ± 0.002. Proteinuria with low specific gravity of 1.012 obtained in this study agreed with the observations of Miles *et al.* (1986) and Chandler *et al.* (2007). Microscopical examination findings were consistent with the opinion of Grauer (2005) who said that persistent proteinuria with inactive urine sediment was the hall mark of glomerular disease.

Urine Protein Creatinine ratio:

The mean UPC value was 4.4 ± 1.91. The international renal interest society (2006) while staging chronic kidney disease have sub staged it based on proteinuria. There were three stages.

Stage 1 with urine protein creatinine value less than 0.2 which was nonproteinuric

Stage 2 where UPC value was between 0.2-0.5 called as borderline proteinuric

Stage 3 with UPC ratio above 0.5 called proteinuric.

The UPC values obtained for all animals in this group were much above normal limit which indicated that all the diseased animals were reported

for treatment much after the onset of disease and it had progressed to such an extent that the changes became irreversible and too advanced.

N-Acetyl-β-D Glucosaminidase (NAG)

Level of urinary NAG index was 15.99 mu/mg of creatinine and 50.91 mu/mg of creatinine on the day of admission. Level of NAG found in this group is consistent with Sato *et al.* (2002) who observed that urinary NAG levels in dogs with chronic kidney disease was 15.7 to 136.8 U/g of creatinine and Langhammer *et al.*(1997)who found increased urinary NAG index in patients with filariasis having tubular and glomerular disorders.

γ Glutamyl transpeptidase (GGT)

Gamma glutamyl transpeptidase levels of two dogs were 3.67 and 7.13 IU/mmol of creatinine. The significant increase in the activity of this renal tubular brush border enzyme indicated that tubular damage was also occurring in microfilarial antigen induced glomerulopathy as observed by Ludders *et al.* (1988) in dogs and Langharnrner *et al.* (1997) in lymphatic filariasis in man.

Alkaline Phosphatase (ALP)

Values of ALP were examined in two dogs and they were 54.29 IU/ mmol and 44.25 IU/ mmol of creatinine. The values obtained were in the high enzyme group as prescribed by Heiene *et al.* (2001). This indicated an extreme degree of tubular damage which occurred along with glomerulopathy according to Ludders *et al.* (1988) and Langhammer *et al. (*1997).

5.3.4 Ultrasonography

The ultrasonographic features indicated infiltrative processes in the renal parenchyma as a result of advanced and prolonged renal disease resulting in fibrosis and replacement of functional renal tissue as reported by

Widmer *et al.* (2004). The diffusedly hyperechoic kidneys with loss of corticomedullary distinction was an indication of end stage kidney . Hyperechoic areas in liver indicated presence of hepatic fibrosis as mentioned by Lamb (1990) which could be a result of multisystem involvement of microfilariosis.

5.3.5 Treatment and response to treatment

Even though all the microfilaraemic dogs responded to treatment with ivermectin by negative blood result within three days it did not result in any clinical improvement as the renal disease was too advanced and irreversible as indicated by Polzin *et al.*(2005) and Grauer (2005). Supportive therapy with fluids, antemetics and antibiotics also did not provide a satisfactory response.

5.3.6 Postmortem and Histopathological Examination

The gross lesions indicated severe chronic nephritis. Extensive damage to tubules, glomeruli and interstitium revealed on histopathology indicated that the disease had progressed to end stage kidney.

Minkus *et al.* (1994) opined that high urine protein values were often the result of glomerular lesions and high creatinine values often related to tubulointerstitial lesions. Since both high creatinine and high UPC ratio were obtained, extensive lesions in all parts of kidney were expected.

5.4 RENAL FAILURE ASSOCIATED WITH PYOMETRA

Heiene *et al.* (2001) observed that pyometra was a chronic infection sometimes complicated by renal lesions of an acute, subacute or chronic nature and which might in some patients progress to uraemia. Polyuria, polydipsia, proteinuria and azotaemia were common features of canine pyometra.

(Heiene *et al.*, 2007). Three cases with pyometra which ended up in renal failure were discussed.

5.4.1 Signalment

Mean age of the affected animals was more in this group (9 years) than that of dogs exposed to nephrotoxins or microfilaraemic dogs and this was consistent with the opinion of Heiene *et al.* (2007) who said that dogs with pyometra were older.

5.4.2 Clinical Observations

The clinical signs were consistent with advanced renal failure. Dogs with pyometra usually have polydipsia and polyuria but two animals in this group had oliguria. It could be because of advanced renal lesions.

5.4.3 Clinical pathology

Haemogram:

The mean haemoglobin concentration, total erythrocyte count, packed cell volume and erythrocyte sedimentation rate on the day of admission were 7.67g% , 3.40 millions./mm^3, 23.70 %, and 74.50 mm/hr respectively. The haemogram indicated a non regenerative anaemia with a guarded prognosis as expected in advanced renal failure (Benjamin,1985). Anaemia observed in the present study might be due to the advanced renal failure and suppression of bone marrow function ((Benjamin,1985).

Leucogram and Platelet count

A stress leucogram as expected in renal failure was observed. The mean leucocyte count was 25433.33/cu mm and neutrophil count was 72.33%. Total leucocyte count was increased but neutrophilia was not marked. Increase of monocytes was noticed in one sample. The mean total leucocyte count reported by Heiene *et al.* (2001) was 22600/cu mm which was in agreement with the present finding.

The mean platelet count on the day of admission was 171000/ mm^3 (98000-242000). There was a marked reduction in platelet count compared to healthy animals. Thrombocytopaenia could be expected as platelet survival was decreased in glomerulonephritis (Grauer, 2005).

Serum Biochemical analysis

Total Protein, Albumin, Globulin and AG ratio

Total protein, albumin, globulin and AG ratio values on the day of admission (with range of values in parenthesis) were 7.5 g/dl (6.8-8.7), 2.47 g/dl (2.3-2.7), 5.03 g/dl (4.1 – 6.4 g/dl) and 0.53 (0.4-0.7) respectively. The values observed were consistent with that of Dabhi and Dhami (2006)

Hyperproteinaemia, hyperglobulinaemia and reduced AG ratio were observed. This was due to the increased globulin production due to chronic antigenic stimulation as a result of the chronic pyometra (Benjamin, 1985) or advanced uraemia, dehydration and toxaemia (Dabhi and Dhami, 2006).

Serum Creatinine, BUN and GGT:

The mean serum creatinine, BUN and GGT levels on the day of admission were 10.90 mg/dl (6.1-15), 133 mg/dl (78-190) and 9.0 (8-10) IU/L

respectively. The value of serum creatinine was much higher than the normal values indicating advanced condition. This was consistent with the findings of Dabhi and Dhami(2006) who noticed that mean serum urea and creatinine were three times higher in affected animals than that of healthy bitches. The occurrence of renal failure in pyometra cases might be due to the immune complex glomerulonephritis and tubular damage induced by toxaemia . In this case the renal lesions were much more advanced and so azotaemia also much more high. Mean blood urea nitrogen level of affected dogs on first day was 133 mg/dl which was in agreement with the findings of Worwag and Langston (2008). Serum GGT was 9.0 (8-10) IU/L on the first day which was within the normal range. De Schepper *et al.* (1989) reported that serum GGT in dogs with pyometra were comparable to control bitches which agreed with the present finding.

Urinalysis:

High proteinuria and isosthenuric specific gravity with inactive sediments and high UPC ratio were noticed. This indicated severe renal involvement (Grauer, 2005). The mean specific gravity was 1.01 which agreed with the findings of Heiene *et al.* (2001) in dogs with pyometra.

Urinary Enzymes

Level of urinary NAG, GGT and ALP were measured in two dogs and the values were 125.94 and 180.72 mu/mg of creatinine, 32.39 IU/m mol and 82.48 IU/mmol of creatinine and 30 and 324.66 IU/ mmol of creatinine respectively.

Urinary NAG, GGT and ALP values were much higher than that of healthy dogs. Similar observation was made by Heiene *et al.* (2001). De Schepper *et al.* (1987) found that renal injury was present in 72 % of bitches with pyometra and increased urinary excretion of protein, GGT and ALP were noticed

in such cases which was consistent with the present finding. This might be due to the immune complex glomerulonephritis and tubular damage induced by *Escherichia coli* endotoxin and the glomerular dysfunction seemed to precede tubular injury. So urinary GGT in bitches with pyometra was a late indication of a more profound degree of renal dysfunction. In pyometra, proximal tubular renal damage developed after glomerular dysfunction and preceding renal failure. (De Schepper *et al.*, 1987).

Sato *et al.* (2002) observed that dogs that had pyometra and exhibited renal insufficiency after ovariohysterectomy showed high values of NAG index before ovariohysterectomy. The authors proposed that urinary NAG index as a good indicator for evaluation of secondary renal disease in pyometra. The present finding also agrees with it.

5.4.4 Ultrasonography:

Enlarged hyperechoic uterus indicated presence of pus in uterus. Medullary rim sign was also present which as reported by Mantis *et al.* (2000) was considered as a nonspecific ultrasonographic sign and this might be a sentinel sign of renal disease. Kidneys were hyperechoic in one dog indicating infiltration of fibrous tissue.

5.4.5 Treatment and Response to treatment

One dog was subjected to ovariohysterectomy which did not cause any improvement in renal function. The routine treatment with fluids, antibiotics, antiemetics and other symptomatic therapy failed to produce any favourable response.

5.4.6 Postmortem and Histopathological Examination

Gross lesions obaserved were small irregular kidney which pits on pressure. Severe haemorrhagic gastroenteritis and haemorrhagic cystitis .

Histopathological lesions suggestive of chronic nephritis were detected. Extensive infiltration, fibrosis, glomerular and tubular sclerosis, cystic dilatation of tubules, multifocal haemorrhage and glomerular haemorrhage were also detected.

Plasmacytic lymphocytic interstitial infiltrates , often with a periglomerular location accompanied by a higher prevalence of interstitial fibrosis and tubular atrophy were the most prominent histological lesions in dogs with pyometra (Heiene *et al.*, 2007) which agreed to the present finding

5.5 RENAL FAILURE ASSOCIATED WITH PROSTATIC ENLARGEMENT

Three animals had prostatic enlargement. Jayathangaraj *et al.* (1993) reported a case of prostatitis with secondary renal failure in a Pomeranian dog aged eight years. Prostatic diseases had been enlisted by Grauer et al.(2005) as a cause of glomerular disease . Another factor related to prostatic enlargement causing renal failure was obstructive nephropathy which causes the functional and pathologic changes in kidney that resulted from obstruction to the flow of urine. It was responsible for approximately 4% of end stage renal failure in human patients (Gloor and Torres, 2007).

5.5.1 Signalment

The dogs with prostatic enlargement and renal failure were comparatively older than other groups. Mean age of affected dogs was 9.33 years with a range of 6-13 years.

5.5.2 Clinical observations

The major clinical signs were lethargy, vomiting, anorexia, oral ulcers, oliguria, melena, posterior paralysis, vomiting, debility, recurrent constipation, dullness, turbid urine and oliguria. These observations were consistent with the findings of Jayathangaraj et al. (1993).

5.5.3 Clinical pathology

Haemogram, leucogram and platelet count showed a pattern similar to that of advanced renal failure discussed earlier. The mean haemoglobin concentration, total erythrocyte count, packed cell volume and erythrocyte sedimentation rate on the day of admission were 11.07 g%, 6.39 millions./mm^3, 43.25 %, and 28.5 mm/hr respectively. Heiene *et al.* (2001) reported that PCV in dogs with renal disorders were 39 % which agreed with the present result.

The mean total leucocyte count on the first day was 20025.00/ mm^3 , neutrophil count 76.50 % (, lymphocyte count 21.50 % and eosinophil count 2 % which indicated a stress leucogram as expected in advanced renal failure.(Benjamin,1985).

Serum Biochemical analysis

Serum creatinine was much higher (10.90mg/dl) than reported by Jayathangaraj *et al.* (1993). The difference in observation might be due to the fact that renal lesions in the present cases were more advanced.

Urinalysis

Urine with specific gravity in isosthenuric range and heavy proteinuria were noticed. Microscopical examination of urine sediments of two cases showed oxalate and triple phosphate crystals. Crystals were often seen in

the urine sediment of normal dogs and cats without much diagnostic significance. (Mikiciuk *et al.*, 1989) One sample had bacteria, erythrocytes and pus cells in normal range suggestive of bacterial infiltration of urinary tract.

Culture and sensitivity

No growth could be obtained on two samples sent for culture and sensitivity examination. In one sample gram negative rods could be found on brain heart infusion agar after 24 hours of incubation. It was sensitive to chloramphenicol (++++), enrofloxacin (+++), gentamicin (+++), cefotaxime (++), nitrofurantoin and resistant to sulphadiazine. The prostatitis in this dog might have caused the urinary tract infection, nephropathy and resultant chronic renal failure.

Urinary enzymes:

Level of urinary NAG, GGT and ALP were measured in two dogs and the values were 456.44 U/g and 21.14 U/g of creatinine, 34.12 IU/m mol and 2.01 IU/mmol of creatinine and 17.14 IU/ mmol of creatinine and 10.71 IU/ mmol of creatinine respectively. All the three enzymes levels in urine were higher than that of normal animals confirming the renal involvement.

5.5.4 Ultrasonography:

Ultrasonographic features consistent with advanced renal failure were seen. Kidney cortex was thick and hyperechoic in one dog and right kidney was affected more. Hyperechoic areas were noticed within the bladder with shadowing. Hyperechoic kidney with reduced corticomedullary distinction in one dog and hypoechoic kidney with hyperechoic areas in both renal pelves in another dog. In all dogs prostate was enlarged and hyperechoic.

5.5.5 Treatment and response to treatment

Even though treatment with fluids, antibiotics, diuretics and antiemetics attempted, all the animals succumbed to the illness. In dogs with obstructive nephropathy,complete recovery was possible only if the obstruction was relieved within one week.The degree of recovery after two and four weeks of obstruction were only 58 and 36 % respectively. No recovery reported after six weeks of obstruction (Vaughan *et al.*, 1971)

5.5.6 Postmortem and Histopathology

Urine outflow obstruction due to enlarged prostate was the common feature. This might have caused postrenal renal failure. Benign prostatic hypertrophy and prostatic tumors were the two diseases causing obstructive nephropathy in human beings(Gloor and Torres,2007).

5.6 RENAL FAILURE ASSOCIATED WITH PANCREATITIS

Two cases of renal failure associated with pancreatitis were investigated. Renal failure secondary to acute pancreatitis is encountered frequently (Williams and Steiner, 2005) The present cases were acute pancreatitis with secondary renal failure as evidenced from the clinical signs and postmortem observations. Cook *et al.* (1993) mentioned renal failure as a risk factor associated with acute pancreatitis and 8 out of 101 dogs with acute pancreatitis had concurrent renal failure.

5.6.1 Signalment

The dogs were a nine year old nondescript castrated male and a ten year old female Labrador. They were both vaccinated against rabies. Multi component vaccine was given only to the Labrador dog. Cook *et al.* (1993) observed that dogs above seven years of age were more prone to pancreatitis and agreed with the present report.

5.6.2 Clinical Observations

The primary complaint of both the dogs was anorexia for a prolonged period (10 and 15 days) and abdominal pain. The temperature, pulse and respiration rates of the dogs were within normal ranges

Visible mucous membranes were pale in both dogs. Lethargy, oliguria, vomiting, ascites and anorexia were seen in both the dogs and melena and oral ulcers in one. Praying posture was noticed in one dog and purulent discharge from eyes noticed in the other dog. Clinical signs observed in these cases were similar to that described by Williams and Steiner (2005). Satake *et al.* (1991) explained that ascitic fluid which accumulated during acute pancreatitis was important in the pathogenesis of renal failure secondary to pancreatitis. About 200 to 400 ml of ascitic fluid was found to be produced within five hours of induction of pancreatitis and an elevation in haematocrit and reduction in mean arterial pressure were also noted indicating hypovolaemia. At the same time renal blood flow, glomerular filtration rate, and urinary output decreased significantly. When sterile ascitic fluid was injected into healthy dogs, hypotension, decreased renal blood flow, decreased glomerular filtration rate and urine output together with increased renal vascular resistance was noticed. The authors continued that renal failure associated with acute pancreatitis occurred mainly as a result of hypovolaemia but also that the sterile ascitic fluid contained nephrotoxic substances.

5.6.3 Clinial pathology

Haemogram

Haemoglobin 6.00 and 5.1 g %, erythrocyte count 3.06 and 2.8 millions /mm^3, PCV 17.2 and 17 % and ESR 5 and 36 mm/hr were the values on the first day. Williams and Steiner (2005) observed that anaemia was a common

manifestation of acute pancreatitis and was in conformity with the present finding.

Leucogram

The leucogram of the animals showed total leucocyte count of 13300 and 8700/ mm^3, neutrophil count of 75 and 69 %, lymphocyte count of 20 and 23 %, eosinophil count of 3 and 7 % and monocyte count of 2 and 1 %. Leucocytosis associated with a left shift is the common hematologic finding in acute pancreatitis (Williams and Steiner, 2005).

Serum biochemical analysis

Total Protein, Albumin, Globulin and A:G ratio

Total protein, albumin, globulin and AG ratio values were 6.2 and 5.12 g/dl, 2.4 and 1.53 g/dl, 3.8 and 3.59 g/dl and 0.6 and 0.42 respectively. These observations agreed with the reports of Muraly (2001), Eubig *et al.* (2005) and Mridula *et al.* (2005).

Serum Creatinine

The mean serum creatinine level on the day of admission was 18 and 26 mg/dl which was in conformity with the observations of Puig *et al.*(1995). The creatinine levels were very high as found in acute renal failure cases.

Blood urea Nitrogen

Blood urea nitrogen level of affected dogs on first day was 154 and 190 mg/dl which agreed with the report of Langstan (2002) suggesting ARF.

Serum Potassium

Serum potassium level on first day was 8.54 and 4.61 m Eq/L

Fasting blood glucose was 132 mg/dl for one animal . For the other animal, fasting blood glucose level was consistently high in the range of 120-160 mg/dl. Serum cortisol 7.1mcg/dl, serum phosphorus 20.4 mg/dl, serum lipase 2340 units, serum cholesterol 194 mg/dl, serum alkaline phosphatase 273 U/l and serum calcium 8 mg% were the other relevant biochemical results.

Hyperglycaemia is common as a result of hyperglucagonaemia, stress related increases in cortisol and catecholamines,or destruction of islet cells by pancreatic inflammation. Hypocalcaemia, hypercholesterolaemia and increases in serum lipase were also associated with pancreatitis. Hyperkalaemia and hyperphosphataemia might have been resulted from acute renal failure (Williams and Steiner, 2005)

Urinalysis

Urine protein was detected on an average of 3+. The specific gravity were 1.01 and 1.015which were in the isosthenuric range.

Urine protein Creatinine Ratio and Urinary Enzymes

Urine protein and creatinine ratio on the day of admission were 9.94 and 2.1 and on seventh day one dog was anuric and UPC of other dog was 2. Urinary enzymes were measured for one dog and the values were NAG 28.21 mu/mg of creatinine, GGT 18.55 IU/mmol of creatinine and ALP 113.48 IU/mmol of creatinine. These values were much higher than the values obtained in healthy dogs which indicated that the animals were in an advanced renal insufficiency.

5.6.4 Ultrasonography

Moderate amount of fluid in abdominal cavity, hypoechoic kidneys with reduced corticomedullary distinction, a hyperechoic mass cranial to kidneys with a localized hypoechoic area in the middle were the important observations in the first dog. In the second dog both kidneys had distorted shape, hyperechoic and reduced corticomedullary distinction.These findings indicated advanced renal failure according to Ponnuswamy *et al.*(2009).

5.6.5 Treatment and response to treatment

Symptomatic treatment with fluids, antibiotics, diuretics and antemetics attempted. Both the animals succumbed to the advanced renal failure. Satake *et al.* (1991) opined that nephrotoxic substances contained in the ascitic fluid were causing the renal damage and they must be removed first for the treatment of acute renal failure secondary to pancreatitis.

5.6.6 Postmortem and Histopathological examination

Postmortem examination of both animals conducted. In one animal the lesions observed were moderate amount of serosanguinous fluid in the abdominal cavity and enlargement of pancreas. Hardened nodular cirrhotic liver, haemorrhagic gastroenteritis, small shrunken and irregular kidneys, pneumonic changes in lungs, fibrin deposits in epicardium and highly hemorrhagic bladder were also observed.

In the other animal, lesions observed were large quantity of serous fluid in pleural cavity with fibrin deposits, collapsed lungs, rounding of heart with hydropericardium, enlargement of left atrium, fibrotic and hard liver, spleen hard in consistency, pancreas enlarged and gritty, and severe haemorrhagic gastroenteritis. Duodenum had severe haemorrhage. Both kidneys were small, irregular with haemorrhagic patches.

The gross postmortem lesions indicated acute pancreatitis, renal failure and associated lesions of multi organ failure.

Histopathological examination showed diffuse lobular-acinar cell necrosis in pancreas and congestion of inter lobular vessels. Islet zone cells were scanty and hyalinized.

In the kidney sections, diffuse interstitial fibrosis, necrosis of some of the glomerulicystic changes and atrophy in some others, tubular degeneration, necrosis and medullary tubular hyalinization were identified.

5.7 RENAL FAILURE ASSOCIATED WITH RHABDOMYOLYSIS

A three year old male weimaraener dog with a history of continous and unusual physical exertion for 4 hours developed acute pain on limbs, later haemoglobinuria and myoglobinuria. On the next day the animal became oliguric, anorectic, collapsed and it was diagnosed as acute renal failure following exertional rhabdomyolysis.

Myoglobinuric acute renal failure may follow any event involving violent and unaccustomed muscular activity. The strenuous exercise caused lactic acid build up in the muscle causing a vascular response which led to muscle ischaemia. The lactic acid build up might be the cause for the pain on limbs. The damage of skeletal muscle could cause release of myoglobin in to the blood stream and due to its relatively small size, readily filterable myoglobin excreted in urine (Porzio *et al.*1997 and Malik,1999).

5.7.1 Clinical observations and pathogenesis

The animal was laterally recumbent. Rectal temperature at the time of presentation was 98 ^{O}F, pulse 96/min and respiration 28/min. The mucous membranes

were congested. The animal was anorectic and had vomiting and the vomitus was blood tinged, oliguria also was noticed. Echymotic patches were seen on the body surface and penile mucosa. The animal was dull, lethargic, having haemoglobinuria and myoglobinuria, icterus, oral ulcers, and muscle weakness. A similar case was reported by Jacobson and Lobetti (1996).The clinical signs were suggestive of oliguric acute renal failure. Myoglobin in the presence of hypovolaemia and aciduria led to the acute renal crisis. Renal vasoconstriction, intrarenal cast formation and heme protein induced nephrotoxicity were the main reasons for ARF in such cases. Fluid third spacing occurred as a result of extravasation to the damaged muscles could cause hypovolaemia and hypoperfusion of kidney. Renal vasodilator nitric oxide was inhibited by myoglobin which could cause renal vasoconstriction and ischaemia. Endotoxin cytokine cascade activated by muscle injury was also a cause for vasoconstriction. Intratubular cast formation causing tubular obstruction depends on the concentration of heme protein and pH of urine. Ferrihemate formed inside the tubules were transported out using ATP causing a reduction in ATP stores of tubular cells which were already hypoxic and injured by renal ischaemia which result in acute tubular damage (Malik, 1999).

5.7.2 Clinical pathology

Haematology , serum biochemistry and urinalysis:

The haemoglobin , RBC count, PCV and ESR of the animal on the day of admission were 17 g%, 6.87 millions/cmm, 56.8 % and 2mm/hour respectively. Increased haemoglobin and PCV observed in the present case which could be due to the effect of dehydration. Total leucocyte count was 38600 /cu mm with differential count of neutrophils 68 %, and lymphocytes 28 %, Eosinophils 2 % and monocytes 2 %.

Platelet count of the animal was 26000/cu mm. The severe thrombocytopaenia could be due to disseminated intravascular coagulation and resulted in widespread echymotic changes. The DIC might be contributed by the thromboplastin release from injured muscles and secondary cofactors including shock, hypoxia and vascular injury (Porzio et al., 1997).

Serum total protein, albumin and globulin were 5.6, 2.7 and 2.9 g /dl respectively. The A:G ratio was 0.7. Serum proteins were in the low normal range and in

6. SUMMARY

The study on "clinico-biochemical and ultrasonographic evaluation of renal failure in dogs" was conducted to investigate the occurrence renal failure in dogs, to study the ultrasonographic findings along with the clinico-pathological observations and to assess the line of therapy.

Dogs presented to the University Veterinary Hospital, Kokkalai and Veterinary College Hospital, Mannuthy with clinical signs suggestive of renal failure such as persistent vomiting, polyuria, oliguria, anorexia, oral ulcers, diarrhea, dehydration and lethargy with serum creatinine level above reference range were selected for the study.

The parameters studied were

Signalment

History and clinical signs

Physical examination findings

Ultrasonography of the kidney

Haematology, serum biochemistry and urinalysis

Urine protein creatinine ratio

Urinary enzymes as markers of renal disease

Treatment and response to treatment

Peritoneal dialysis as a treatment option

Postmortem examination and histopathology

A total of 23 cases were selected for the study. Majority of them were well maintained dogs in the age group of 4-8 years. The breeds represented were German shepherd, Nondescript, Labrador, Doberman, Neapolitan mastiff, Spitz, Dalmatian, Weimaraner, and Rottweiler.

Lethargy, anorexia, vomiting, melena, oliguria, muscle weakness, polyuria and oral ulcers were the important clinical signs of renal failure observed in this study. Less prominent signs included jaundice, ascites, oedema, exercise intolerance, and haemoglobinuria.

rhabdomyolysis, hypoproteinaemia and hypoalbuminaemia could be expected due to the loss of plasma components owing to capillary damage (Haburjack and Spangler, 2002).

Serum creatinine was 5.6 mg/dl and BUN 123 mg/dl. Azotaemia is expected in rhabdomyolysis due to the haemoconcentration as well as acute renal failure .An elevation of the ratio of serum creatinine to BUN (1:10) could be seen in rhabdomyolysis. This was due to the fact that the large quantity of creatine produced from the damaged muscle is spontaneously dehydrated to creatinine leading to rise in serum creatinine alone and change the ratio (Malik, 1999).

Other biochemical parameters were bilirubin 1.4mg/dl, serum alkaline phosphatase 122 IU/L, serum potassium 5 mEq/L ,serum GGT 38 IU/L, serum AST 2390 IU/L, serum ALT 1003 IU/L and serum creatine phosphokinase 55000IU/L. Creatine phosphokinase MM isoform is present in skeletal muscle and on damage to the muscles resulted in the release of this enzyme into the blood. Rise in AST might also be due to skeletal muscle damage. Marked increase in ALT, bilirubin and GGT might be due to hepatocellular and cholestatic damage (Porzio *et al.* 1997).

Specific gravity of urine was 1.007 and the urine sample was positive for myoglobin, protein, glucose and bile pigments. Specific gravity of urine in the hyposthenuric range even in the presence of myoglobin, protein, glucose and bile pigments indicated severe renal damage (Benjamin, 1985).

5.7.3 Ultrasonography

On ultrasound scanning both kidneys were hypoechoic with no corticomedullary distinction. The liver parenchyma was hypoechoic and the gall bladder was shrunken. The portal veins were dilated. The ultrasound picture indicated severe renal and hepatic damage.

5.7.4 Treatment and Treatment response

The animal was treated with parenteral fluids, Inj amoxicillin and cloxacillin @20 mg/kg body weight and Inj calcium gluconate @1 ml/kg body wt

I/V.The animal did not respond to the treatment and died on the fifth day of presentation. Postmortem examination could not be conducted. Diagnosis of rhabdomyolysis should be made at the earliest and aggressive fluid therapy followed by a forced alkaline diuresis was indicated before the onset of irreversible ARF (Malik,1999)

5.8 RENAL FAILURE ASSOCIATED WITH LEPTOSPIROSIS

A nondescript male dog aged 1.5 years was presented with the history of continuous vomiting. It was not vaccinated with prophylactic antirabies vaccine or multicomponent vaccine. Even in vaccinated animals occurrence of leptospirosis was not uncommon (Birnbaum *et al.*,1998). The animal was oliguric, having difficulty to stand up, was having shaking movement of head while standing, had diarrhea since one day, anorectic and lethargic.The temperature was 100.4°F, pulse 76/min, respiration 24/min and the visible mucous membranes were congested.

Birnbaum *et al.*(1998) on analysis of 36 cases of leptospirosis found that the median age was 7.4 years with range of 2 months to 13 years. The most common signs reported by them were anorexia, lethargy, depression, polyuria, polydypsia and vomiting. Weight loss, weakness, diarrhea, musculoskeletal pain, disorientation, anuria, stranguria, adipsia, haematochezia, haematuria, melena and dyspnoea and was in conformity with signs seen in the present case. Icterus was seen only in 11% of the cases by the authors.

5.8.1 Clinical pathology

Haematology , serum biochemistry and urinalysis:

Haemoglobin, erythrocyte count, VPRC and ESR were 10.3 g/dl, 6.23 millions/cmm, 32.6 %, and 10mm/hour respectively on the first day and the corresponding values on seventh day were 10.2, 6.6, 31 and 26 respectively. Birnbaum *et al.*(1998) noticed a mild nonregenerative anaemia in 33 % of affected dogs.

The total leucocyte count was 64600/cmm, with neutrophils 80%, lymphocytes 15 %, eosinophil 1 % and monocyte 4 % .Platelet count was 128000/cu mm. On seventh day these values were 72400/cumm, 82%, 15%, 2%, 1% and 242000/cumm respectively.

Indu *et al.* (2001) reported a case of leptospirosis in a dog and the clinical signs observed were in agreement with the present case. Severe leucocytosis with neutrophilia is expected in a case of leptospirosis. According to Birnbaum *et al.*(1998) , 31% of the dogs examined by them showed leucocytosis characterised by a mature neutrophilia which is agreeing with the present finding.

Miller *et al. (2007)* .found that animals with a stress leucogram with leucocytosis, neutrophilia, monocytosis and eosinopenia as in the present case were less likely to survive .The authors also suggested that renal failure was the typical response to leptospiral infection in an unadapted host such as dog. Following localization in the renal tubules, it is proposed that leptospiral toxins cause necrosis of adjacent tubular cells with resultant nephrosis and subsequent renal failure.

Thrombocytopaenia may be associated with platelet aggregation due to the action of leptospiral lipopolysaccharide but could indicate impending or concurrent DIC (Miller *et al.*(2007).

The total protein, albumin, globulin and AG ratio were 5.3 g/dl, 2.3 g/dl, 3 g/dl, 0.76 respectively on the first day. The same parameters on seventh day were 4.27 g/dl, 1.59 g/dl, 2.68 g/dl and 0.59 respectively and the changes indicated a deterioration in condition. This was in conformity with finding of Birnbaum *et al.*(1998) and Indu *et al.*(2001).

Serum creatinine was 11.23 mg/dl on first day and 18 mg/dl on seventh day. Blood urea nitrogen was 256 mg/dl and 372 mg/dl on first and seventh day respectively. Birnbaum *et al.* (1998) reported that azotaemia was a common finding in leptospirosis due to the renal involvement.

Urinalysis revealed the following results. Specific gravity was 1.010 and 1.015 on first and seventh days. Protein was 3+, and blood was also present moderately. Urine protein creatinine ratio was 13.54. The urinary NAG was 124.16 mu/mg of creatinine, urinary GGT was 4.49 IU/mmol of creatinine and urinary alkaline phosphatase was 42.62 IU/mmol of creatinine. The urine on dark field microscopy showed leptospiral organisms.

***5.8.2* Ultrasonography:**

On ultrasonography left kidney hyperechoic, right kidney distended and corticomedullary junction was indistinct. These findings indicated an advanced renal disease according to ponnuswamy *et al.*,(2009).

5.8.3 Treatment and response to treatment

The animal was treated with Benzyl Penicillin intravenous injection along with parenteral fluids, (Inj Normal Saline IV) and antemetics (Inj Metoclopramide@ 0.2-0.4 mg/kg SC). The animal did not respond and died on the ninth day of admission. The treatment of leptospirosis should be initiated before the lesions in kidney are not too advanced and became irreversible. The present case and that reported by Indu *et. al.* (2001) were similar in that the disease were too advanced at the time of presentation and hence treatment was not effective.

Summary

6. SUMMARY

The study on "clinico-biochemical and ultrasonographic evaluation of renal failure in dogs" was conducted to investigate the occurrence renal failure in dogs, to study the ultrasonographic findings along with the clinico-pathological observations and to assess the line of therapy.

Dogs presented to the University Veterinary Hospital, Kokkalai and Veterinary College Hospital, Mannuthy with clinical signs suggestive of renal failure such as persistent vomiting, polyuria, oliguria, anorexia, oral ulcers, diarrhea, dehydration and lethargy with serum creatinine level above reference range were selected for the study.

The parameters studied were

Signalment

History and clinical signs

Physical examination findings

Ultrasonography of the kidney

Haematology, serum biochemistry and urinalysis

Urine protein creatinine ratio

Urinary enzymes as markers of renal disease

Treatment and response to treatment

Peritoneal dialysis as a treatment option

Postmortem examination and histopathology

A total of 23 cases were selected for the study. Majority of them were well maintained dogs in the age group of 4-8 years. The breeds represented were German shepherd, Nondescript, Labrador, Doberman, Neapolitan mastiff, Spitz, Dalmatian, Weimaraner, and Rottweiler.

Lethargy, anorexia, vomiting, melena, oliguria, muscle weakness, polyuria and oral ulcers were the important clinical signs of renal failure observed in this study. Less prominent signs included jaundice, ascites, oedema, exercise intolerance, and haemoglobinuria.

After clinical examination, the cases were classified. Exposure to nephrotoxic drugs (n=9), microfilariosis (n=4), pyometra (n=3), enlargement of prostate (n=3), pancreatitis (n=2), Rhabdomyolysis (n=1) and Leptospirosis (n=1) were found to be associated with renal failure.

Nephrotoxic instances observed were prolonged and simultaneous treatment with ivermectin, oxytetracycline, gentamicin, meloxicam and ceftriaxone. These nephrotoxic drugs were administered either as combinations or as single drugs. Many a times animals with subclinical renal disease, were presented with clinical signs such as diarrhea or vomiting (causing dehydration). When they were treated with nephrotoxic drugs, it could result in "acute on chronic renal failure".

Microfilariosis is a very common condition in the dogs of Kerala and its presence in blood was causing prolonged antigenic stimulation resulting in glomerulonephritis which when undiagnosed and not treated led to renal failure.

Pyometra is an important gyanaecological problem among the female dogs of the state and it was found that in many cases it was culminating in renal failure due to the *Escherichia coli* endotoxin induced tubular and interstitial damage and immune mediated glomerulonephritis.

It was found in this study that prostatic enlargement was a common condition and many a times it ended up in renal failure due to obstructive nephropathy. Cases of pancreatitis, rhabdomyolysis and leptospirosis also led to renal failure.

The haematological and biochemical parameters showed sharp differences from reference values. Comparison of first day and seventh day values did not significantly differ indicating that the treatment was not effective. Serum creatinine and BUN, indicators of renal damage crossed the reference range only when the disease was so advanced that 75% of the nephrons were damaged. Almost all cases in the present study were having serum creatinine levels more than 10mg/dl indicating that more than 90% of the nephrons had already been lost making it an irreversible condition.

The ultrasonographic pattern indicated hyperechoic kidneys with reduced or lack of corticomedullary distinction suggesting marked renal fibrosis and irreversible damage. Urinalysis and urinary enzyme estimation also indicated severe injury to the renal parenchyma. Urinary brush border enzymes GGT and ALP and lysosomal enzyme NAG were used as early markers of renal disease. Since the animals were in an advanced state of uraemia, no effective treatment could be instituted except symptomatic therapy which also proved to be ineffective.

Peritoneal dialysis was tried as treatment option in six cases. Even though no significant improvement was noticed the apparent reduction in azotaemia even in end stage renal disease indicates that if used early in the course of disease, it could prove to be an effective alternative for managing acute renal failure cases. Further studies are required in this aspect.

On postmortem and histopathological examination, all the cases revealed lesions of end stage kidney where a reversal was impossible.

From this study it was concluded that

1. Renal failure was a common condition among the dogs of Trichur and neighbouring districts and many cases were iatrogenic
2. Renal failure was diagnosed very late so that a reversal of the condition or betterment of the quality of life of the pet was often impossible.
3. Ultrasonographic finding of hyperechoic kidneys with lack of corticomedullary distinction correlate often with advanced uraemia.
4. Evaluation of renal health is a must while treating conditions such as microfilariosis, pyometra, and prostatic enlargement or before administering nephrotoxic drugs.
5. Renal function should be evaluated in all clinical conditions with signs suggestive of renal involvement.

6. Estimation of urine specific gravity and proteinuria should be made a routine practice to identify subclinical renal disease.
7. Urine protein creatinine ratio, urinary NAG, GGT and ALP can be used as early markers of renal disease.

References

REFERENCES

Ali-Miraftab, H., Bourbouze , R., Bondiou,M.T. and Percheron,F. 1988.Urinary excretion of N-acetyl--beta D-glucosaminidase (NAG) and its isoenzyme B as a marker of the nephrotoxicity of gentamicin: Retest from an animal model. *Pathol. Biol.* (Paris).36:240-244

Albasan, H., Lulich, J.P.and Osborne, C. A. 2003. Effects of storage time and temperature on pH, specific gravity and crystal formation in urine samples from dogs and cats.*J.Am.Vet.Med.Assoc.*.222:176-179.

[Anonymous] 2006.AAHA Canine vaccine Guidelines, RevisedAmerican Animal Hospital Association. http://www.aahanet.org/PublicDocuments/VaccineGuidelines06Revised.pdf.

[Anonymous] 2004.*17th Quinquennial livestock census in Kerala.* Department of Animal husbandry. Available: http://ahdkerala.gov.in/census.pdf

[Anonymous].2006. Iris2006-Staging of CKD (available online) http://www.iris-kidney.com/guidelines/en/staging_ckd.shtml

Antony,S.2004. *Ultrasonographic investigation of urinary tract disorders in dogs.* M.V.Sc.Thesis submitted to the Kerala Agricultural University,Trichur p 96.

Armbrust, L.J., Biller, D.S., Hoskinson, J.J., Meier, H.T. and Michiels, M.L. 2001. The basics of renal ultrasonography.*Vet.Med.*2:114-132.

Bancroft, J.D. and Cook, H.C.1984.*Manual of Histological Techniques.*2nd Ed. Churchill Livingstone, Edinburg.pp18-25

Barr, F.J., Holt, P.E. and Gibbs, C.1990. Ultrasonographic measurement of normal renal parameters.*J.Small.Anim.Pract.*31:180-184.

Bell, R., Borjesson, B., Wolf, P. 1984. Quantitative morphological studies of aging changes in the kidney of the Lewis rat. *Renal Physiol.* 7: 176-184

Benjamin, M.M.1985. *Outline of Veterinary Clinical Pathology.* 3rd Ed. Indian reprint. Kalyani Publishers, New Delhi.p.351

Birnbaum, N., Barr, S.C., Center, S.A., Schermerhorn, T., Randolph, J.F. and Simpson, K.W.1998. Naturally acquired leptospirosis in 36 dogs: Serological and clinicopathological features.*J.Small.Anim.Pract.*39:231-236

Biewenga,W.J. and Van der Brom,W.E.1981. Assessment of glomerular filtration rate in dogs with renal insufficiency: analysis of the cr-EDTA clearance and its relation to the plasma concentration of urea and creatinine.*Res.Vet.Sci.*30:158-160

Bourgoignie, J.J., Gavellas, G., Martinez, E. and Pardo, V. 1987. Glomerular function and morphology after renal mass reduction in dogs. *Laboratory Clinical Medicine* 109: 380-388

Braun,J.P.,Lefebvre,H.P. and Watson,A.D.J. 2003. Creatinine in the dog: a review. Vet.Clin.Pathol. 32:162-179

Brenner, B.M., Meyer, J.W. and Hostetter, T.H. 1982. Dietary protein intake and the progressive nature of renal disease. The role of hemodynamically mediated glomerular injury in the pathogenesis of progressive glomerular sclerosis in aging, renal ablation and intrinsic renal disease. *New England Journal of Medicine* 307: 652-659

Brown, S.A. 1985. Gentamicin associated acute renal failure in the dog. *J.Am.Vet.Med.Assoc.*. 186: 686-690

Brown, S.A., Crowell, W.A., Brown, C.A., Barsanti, J.A. and Finco, D.R. (1997). Pathophysiology and management of progressive renal disease. *The Veterinary Journal* 154: 93-109

Bruchim, Y., Klement, E., Saragusty, J., Finkeilstein, E., Kass, P. and Aroch, I. 2006.Heat stroke in dogs: A retrospective study of 54 cases (1999-2004) and analysis of risk factors for death.*J.Vet.intern.Med.*20:38-46.

Brunker, J.D., Ponzio, N.M. and Payton, M.E.2009.Indices of urine N-acetyl-β-D-glucosaminidase and γ-glutamyl transpeptidase activities in clinically normal adult dogs. *Am.J.Vet.Res.* 70(2):297-301.

Bryan, J. N., Henry, C. J., Turnquist, S. E., Tyler, J. W., Liptak, J. M., Rizzo, S. A., Sfiligoi, G., Steinberg, S. J., Smith, A. N. and Jackson, T. 2006. Primary renal neoplasia of dogs. *J.Vet.Intern.Med.*20:1155-1160

Center, S.A. 1985. 24-Hour urine protein creatinine ratio in dogs with protein losing nephropathies. *J.Am.Vet.Med.Assoc.*187 (8):820-823

Center, S.A., Smith, C.A., Wilkinson, E., Erb, H.N. and Lewis, R.M.1987.Clinicopathologic renal immuno fluorescent and light microscopic features of glomerulonephritis in the dog: 41 cases (1975-1985). *J.Am.Vet.Med.Assoc.*190 (1):81-89

Chandler, M.L., Elwood, C., Murphy, K.F., Gajanayake, I. and Syme, H.M. 2007. Juvenile nephropathy in 37 boxer dogs. *J. Small Anim. Pract.* 48: 690-694

Cook J.H., Rosenfield, A.T. and Taylor, K.J.W.1977. Ultrasonographic demonstration of internal anatomy.*Am.J.Rontgenol.*129:831-835]

Cook,A.K.,Breitschwerdt,E.B.,Levine,J.F.,Bunch,S.E. and Linn,L.O.1993. Risk factors associated with ac pancreatitis in dogs:101 cases(1985-1990) *J.Am.Vet.Med.Assoc.* 203:673-679

Cortadellas, O., Palacio, M.J.F., Bayon, A., Albert, A., and Talavera, J.2006. Systemic Hypertension in Dogs with Leishmaniasis: Prevalence and Clinical Consequences. *J.Vet.Intern.Med.*20:941-947

Cowan, K.A. and Ling, G.V.1981.Results of urinalysis and bacterial culture of canine urine obtained by ante pubic cystocentesis, catheterization and mid stream voided methods. *J.Am.Vet.Med.Assoc.* 179(9):891-894

Cowgill,L.D. and Francey,T. 2005. Acute Uremia.In: *Textbook of veterinary internal medicine. Diseases of the dog and cat.*6th ed. Ettinger, S.J. and Feldman,E.C.(Eds)Elsevier Saunders. St.Louis, Missouri. pp1731-1751

Cruickshank, R., Duguid, J.P., Marmion, B.P. and Swain, R.H.A.1975.Cultural pattern of bacteria. *Medical Microbiology.*12th ed.Churchill Livingstone, Edinburgh. p.920

Dabhi, D. M. and Dhami, .M. 2006 .Serum urea,creatinine,cholesterol, and protein profile in bitches with pyometra.*Indian.Vet.J.*1182-1185.

*De Schepper,J.,Van der Stock,J.,Capiau,E. and de Cock,I.1987. Renal injury in dogs with pyometra.*Tijdschr. Diergeneeskd.* 112:1245-1265

De Schepper,J., De Cock,I. and Capiau,E.1989.Urinary gamma glutamyl transferase and the degree of renal dysfunction in 75 bitches with pyometra.*Res.Vet.Sci.*46:396-400

Deguchi, E. and Akuzawa, M. 1997. Renal clearance of endogenous creatinine, urea, sodium, and potassium in normal cats and cats with chronic renal failure.*J.Vet.Med.Sci.*59 (7):509-512.

DiBartola,S.P.2005. Renal disease: Clinical approach and laboratory evaluation.In:*Textbook of veterinary internal medicine Diseases of the dog and cat* 6th Ed.Ettinger,S.J. and Feldman,E.C.(Eds).Elsevier Saunders,Missouri. p 1991

Dorval, P. and Boysen, S.R. 2007. Management of acute renal failure in cats using peritoneal dialysis: a retrospective study of six cases (2003-2007).*Journal of feline medicine and surgery.*6:4-9.

*Doumasa, B.T.1971.*Cain.Chim.Acta.*31:87 Cited from the operation instructions of the reagent kit for estimation of albumin.

Doxey, D.L.1983.Clinical and Laboratory diagnosis of renal disease. In. *Veterinary Nephrology* Hall, L. and Heinemann, W(Eds)Veterinary books. London, p365

Doxey, J.E., Mc Caw, D.L. and Mikiciuk, M.G. 1989. Managing dogs with glomerular disease. *Vet. Med.* 3: 304-306

Drake, J.C. 1965. Some aspects of kidney physiology and pathology. *J. Small. Anim. Pract.* 6: 273-277

Ebisawa, T., Uechi, M., Hori, Y. and Yamano, S. 2006. Short term change of urinary N-acetyl-β-D-glucosaminidase in reduced kidney mass with renal artery ligation. *J.Vet.Med.Sci.*68 (12):1355-1357

Eubig, P.A., Brady, M.S., Sharon, M., Brant, G., Khan, A.S., Mazzaferro, E.M., and Morrow, C.M.K. 2005. Acute Renal Failure in Dogs after the Ingestion of Grapes or Raisins: A Retrospective Evaluation of 43 Dogs (1992–2002) *J. Vet. Intern. Med.* 19:663–674

Fang, H.C., Lee, P.T., Lu, P.J., Chan, C.L., Chang, T.Y., Hsu, C.Y., Chung, H.M. and Chou, K.J. 2008. Mechanisms of star fruit induced acute renal failure. *Food and Chemical Toxicology* 46: 1744-1752

Finco,D.R.1995. Congenital,inherited,and familial renal disease. In: *Canine and feline Nephrology and Urology.* Osborne, C.A. and Finco, R.(Eds.) Williams and Wilkins.USA. p 483

Fleming,E.J.,McCaw,D.L. and Mikiciuk,M.G.(1989).Managing dogs with glomerular disease.*Vet.Med.*3:304-306

Forrest,L.J., O'Brien,T., Tremelling,M.S., Steinberg,H., Cooley,J. and Kerlin,R.L.1998.Sonographic renal findings in 20 dogs with leptospirosis. *Vet.Radiol & Ultrasound.*39:337-340

Forrester, D.S. and Brandt, K.S. 1994. The diagnostic approach to the patient with acute renal failure. *Vet. Med.* 3: 212-218

Forrester, S.D., Jacobson, J.D. and Fallin, E.A. 1994(b). Taking measures to prevent acute renal failure. *Vet. Med.* 3: 231-236

Forrester, D.S. and Little, S.E. 1994(c). The etiopathogenesis of acute renal failure. *Vet. Med.* 3:202-211.

Gary, T.A., Cohn, L.A., Kerl, M.E. and Jensen, W.A.2004.The effects of exercise on urinary albumin excretion in dogs.*J.Vet.Intern.Med.*18:52-55

Gleadhill, A. (1994) Evaluation of screening tests for renal insufficiency in the dog. *J. Small Anim. Pract.* 35: 391-96

Gloor, J.M. and Torres,V.E.2007.Reflux and obstructive nephropathy. In: *Atlas of the diseases of kidney.*Schrier(Ed).Available online. http://www.kidneyatlas.org/toc.htm

Goldstein, R. E., Lin, R.C., Langston, C.E., Scrivani, P.V., Erb, H.N. and Barr, S.C.2006. Influence of Infecting Serogroup on Clinical Features of Leptospirosis in Dogs. *J Vet Intern Med* .20:489–494

Gopegui, R.R.D., Espada, Y. and Majo, N. 1999. Bilateral hydroureter and hydronephrosis in a nine year old female German Shepherd dog. *J. Small Anim Pract.* 40: 224-226

*Gornall, A.G., Bardawill, C.J. and David, M.M.1949. Determination of serum protein by means of biuret reaction.*J.Biol.Chem.* 177:1751-1752

Gosset,K.A.,Turnwald,G.H.,Kearney,M.T.,Greco,D.S. and Cleghorn,B.O.1987.Evaluation of γ glutamyl trans peptidase to creatinine ratio from spot samples of urine supernatant,as an indicator of urinary enzyme excretion in dogs. *Am.J.Vet.Res.* 148:455-457

Grauer, G.F. 1992. Effects of dietary protein conditioning on gentamicin induced nephrotoxicity in dogs. *J. Am. Soc. Nephrol.* 3: 724

Grauer, G.F. 2005. Canine glomerulonephritis: new thoughts on proteinuria and treatment. *J. Small Anim. Pract.* 46: 469-478

Grauer, G.F., Thomas, C.B. and Eicker, S.W.1985. Estimation of quantitative proteinuria in the dog using the urine protein to creatinine ratio from a random voided sample. *Am.J.Vet.Res.* 46(10):2116-2119

Grauer, G.F., Greco, D.S., Getzy, D.M., Cowgill, L.D., Vaden, S.L. and Chew, D.J. 2000. Effects of Enalapril versus placebo as a treatment for canine idiopathic glomerulonephritis. *J.Vet. Intern. Med* .14:526–533.

Greco, D.S. 1985. Urinary γ glutamyl transpeptidase activity in dogs with gentamicin induced nephrotoxicity. *Am.J.Vet.Res.* 46: 2332-2335.

Greene,C.E.and Schultz,R.D. 2005. Immunoprophylaxis. Infectious diseases of the dog and cat. Ed. Greene,C.E. W.B.Saunders, Philadelphia.pp1069 – 1118.

Haburjak, J.J. and Spangler, W.L.2002.Isoniazid induced seizures with secondary rhabdomyolysis and associated acute renal failure in a dog.*J.Small.Anim.Pract.*43:182-186

Haers, H. and Saunders, J.H. 2009. Review of clinical characteristics and applications of contrast – enhanced ultrasonography in dogs. *J.Am.Vet.Med.Assoc.* 234(4):460-470.

Heiene, R., Biewenga, W.J. and Koeman, J.P. 1991.Urinary alkaline phosphatase and γ-glutamyl transferase as indicators of acute renal damage in dogs.*J.Small.Anim.Pract.*32:521-524

Heiene, R. Moe, L. and Molmen, G. 2001. Calculation of urinary enzyme excretion, with renal structure and function in dogs with pyometra. *Research in Veterinary Science* 70: 129-137.

Heiene,R.,Kristiansen,V.,Teige,J. and Jansen,J.H.2007. Renal histomorphology in dogs with pyometra and control dogs, and long term clinical outcome with respect to signs of kidney disease. *Acta. Vet. Scand.*49:13 Available:http://www.actavetscand.com/content/49/1/13

Hollowway, A. and O'Brien, R. 2007. Perirenal effusion in dogs and cats with acute renal failure. *Radiology & Ultrasound.* 48(6):574-579.

Humes, H.D. 1984. Calcium is a competitive inhibitor of Gentamicin. Renal membrane binding interactions and dietary calcium supplementation protects against gentamicin nephrotoxicity. *J. Clin. Invest.* 73: 134-147

Hutton, T.A., Goldstein, R.E., Njaa, B.L., Atwater, D.Z. and Simpson, K.W. 2008. Search for *Borrelia burgdorferi* in kidneys of dogs with suspected "lyme nephritis". *J.Vet.Intern.Med.*22:860-865

Indu,S.,Saseendranath,M.R.,Baby,K.,Venkataraman,K.S.,Jayakumar,K.M. and Balakrishnan,V.S. 2001.Acute leptospirosis in a dog-a case report.*J.Vet.Anim.Sci.*32:65-66

Ivancic,M. and Mai,W. 2008. Qualitative and quantitative comparison of renal vs hepatic ultrasonographic intensity in healthy dogs. *Vet.Radiol. & Ultrasound.*4:368-373

Jacobson, S.L. 2006. The South African form of severe and complicated canine babesiosis: Clinical advances 1994-2004. *Vet. Parasitol.* 138: 126-139

Jacobson,L.S. and R.G.Lobetti.1996.Rhabdomyolysis as a complication of canine babesiosis. *J.Small.Anim.Pract.*37:286-291

Jayathangaraj, M.G., Srinivasan, S.R. and Ayyappan, S. 1993. Prostatitis and secondary acute renal failure in a dog- Case report. *Indian.Vet.J.* 70:386-387.

Keenan, K.P., Alexander, A.D. and Montgomery, C.A.1978. Pathogenesis of experimental *Leptospira interogans, serovar bataviae,* infection in the dog: Microbiological, clinical, hematologic and biochemical studies. *Am.J.Vet.Res.* 39:449-454.

Kelly, D.F. 1967. Aspects of canine renal pathology. *J. Small Anim. Pract.* 8: 329-335.

Kessler, M. 2008. Secondary polycythaemia associated with high plasma erythropoietin concentrations in a dog with a necrotizing pyelonephritis. *J. Small Anim. Pract* 49: 363-366

[Anonymous]1996. Editorial review.Rhabdomyolysis and myohaemoglobinuric acute renal failure. *Kidney international.*49:314-326.

Kirby, R. 1989. Acute renal failure as a complication in the critically ill animal. *Vet. Clin. North. Am.* 19: 1189-1208

Kitagawa, H., Sasaki, Y., Ishihara, K. 1989. Clinical studies on canine dirofilarial haemaglobinurea: measured and calculated serum osmolatities and osmolar gap. *Jap. J. Vet. Sci.* 51(4): 703-710.

Konde, L.J., Wrigley, R.H., Park, R.D. And Lebel, J.L.1984.Ultrasonographic anatomy of normal canine kidney.*Vet.Radiol.*25:173-178.

Kraje, A.C. 2002. Helping patients that have acute renal failure. *Vet. Med.* 4:461-474

Kuwahara, Y., Ohba, Y., Kitoh, K., Kuwahara, N. and Kitagawa, H. 2006. Association of laboratory data and death within one month in cats with chronic renal failure. *J.Small.Anim.Pract.*47:446-450.

Lamb, C.R.1990. Abdominal ultrasonography in small animals: Intestinal tract and mesentery, kidneys, adrenal glands, uterus and prostate.*J.Small.Anim.Pract.*31:295-304.

Langhammer, J., Birk, H.W., and Zahner, H. 1997.Renal disease in lymphatic filariasis:evidence for tubular and glomerular disorders at various stages of infection. *Tropical medicine and International Health.* 9:875-884.

Langstan,C.E. 2002.Acute renal failure caused by lily ingestion in 6 cats.*J J.Am.Vet.Med.Assoc.* 220:49-52

Langston, C. 2003.Advanced renal therapies: Options when standard treatments are not enough. *Vet.Med.* 12: 999-1006.

Lees,G.F.,Brown,S.A.,Elliott,J.,Grauer,G.F. and Vaden,S.L.2005.Assessment and management of proteinuria in dogs and cats:2004 ACVIM forum consensus statement(small animal).*J.Vet.Intern. Med.*19:377-385

Leibetseder, J.L. and Neufield, K.W. 1991.Effects of dietary protein and phosphorus levels in dogs with chronic renal failure.In: *Proceedings of the Purina international nutrient symposium*, Oriando, Florida, USA.pp 35-38.

Leifer, C.E., Page, R.L., Matus, R.E., Patnaik, A.K. and MacEwen, E.G. 1987. Proliferative glomerulonephritis and chronic active hepatitis with cirrhosis associated with *Corynebacterium parvum* immunotherapy in a dog. *J.Am.Vet.Med.Assoc.* 190(1):78-80.

Locke, J.E., and Barber L.G. 2006. Comparative aspects and clinical outcomes of canine renal hemangiosarcoma. *J. Vet. Intern. Med* .20:962–967

Ludders, J.W., Grauer, G.F., Dubielzig, R.R., Ribble, G.A., Wilson, J.W.1988.Renal microcirculatory and correlated histologic changes associated with dirofilariasis in dogs.*Am.J.Vet.Res.*49:826-30.

Maddison,J.E. and Johnston,K.A.2002 .Non steroidal anti-inflammatory drugs and chondroprotective agents In:*Small animal clinical pharmacology.* Maddison,J.E.,Page,S.W. and Church,D.(Eds)W.B.Saunders,Philadelphia.p547

Maddison,J.E. and Watson,A.D.J.2002 .Antibacterial drugs.In:*Small animal clinical pharmacology.* Maddison,J.E.,Page,S.W. and Church,D.(Eds)W.B.Saunders,Philadelphia.p547

Malik,G.H.1999.Rhabdomyolysis and myoglobin induced acute renal failure.*Saudi.J.Kidney.Dis.Transplant.*9:273-284

Mantis,P.and Lamb,C.R. 2000.Most dogs with medullary rim sign on ultrasonography have no demonstrable renal dysfunction.*Veterinary Radiology & ultrasound,*41:164-166

Mareschal, A., Anjou, M.A., Moreau, M., Alexander, K. and Beauregard.G. 2007. Ultrasonographic measurement of kidney to aorta ratio as a method of estimating renal size in dogs. *Radiology & ultrasound.* 48(5):434-438.

*Marsh, W.H., Figurhut, B. and Miller,H.1965.Operation instructions of the reagent kit to estimate blood urea.*Clin.Chem.*11:624

Mathews, K.A. and Monteith, G. 2007. Evaluation of adding diltiazem therapy to standard treatment of acute renal failure caused by leptospirosis: 18 dogs (1998-2001). *Journal of Veterinary Emergency and Critical care* 17(2): 149-158

Mc Caw, D.L., Fleming, E.J. and Mikiciuk, M.G. 1989(a). Selecting the right diagnostic tests for renal disease. *Vet.Med.* 3:266-272

McCaw, D.L., Fleming, E.J. and Mikiciuk, M.G. 1989(b). Interpreting the results of urinalysis: A key to diagnosing renal disorders.*Vet.Med.*3:281-286

Medaille, C., Trumel, C., Concordet, D., Vergez, F. and Braun, J.P. 2004. Comparison of plasma/serum urea and creatinine concentrations in the dog: A 5 year retrospective study in a commercial veterinary clinical pathology laboratory. *J.Vet.Med.* 51:119-123

Meynard, J.A. 1975. Traumatic rupture of the bladder in the dog-a clinical study of nine cases. *J. Small Anim. Pract.* 2: 131-134.

Mikiciuk, M.G., Fleming, E.J. and McCaw, D.L.1989.Chronic renal failure in dogs: Managing an irreversible condition.*Vet.Med.*3:297-303

Miles, C.A., Feher, C.R. and Cohen, D.R. 1986. Juvenile onset renal disease in Doberman Pinschers. *Vet. Med.* 12: 1106-1111

Miller,R.I., Ross,S.P., Sullivan,N.D. and Perkins,N.R. 2007.Clinical and epidemiological features of canine leptospirosis in North Queensland. *Aust.Vet.J.*85:13-19.

Minkus,G.,Reusch,C.,Horauf,A.,Breuer,W.,Darbes,J.,Kraft,W. and Hermanns,W.1994.Evaluation of renal biopsies in cats and dogs-histopathology in comparison with clinical data.*J.Small.Anim.Pract.*35:465-472

Mishina, M., Watanabe, T., Fuji, K., Maeda, H. and Wakao, Y. 2000. Medical dissolution of struvite nephrolithiasis using amino acid preparation in dogs. *J.Vet.Med.Sci.* 62(8):889-892

Morrow,C.K.M.,Valli,V.E,Volmer,P.A. and Eubig,P.A.2005. Canine renal pathology associated with grape or raisin ingestion:10 cases.*J.Vet.Diagn.Invest.*17:223-231

Moustafa, A.M., Agag, B., Esmat, M., Selim, A.M. 1991. Studies on filariasis in Egyptian buffaloes. III.Clinical observations and electrophoretic patterns in sera of naturally infested buffaloes with microfilaria before and after treatment with Stipophon. *Zagazig Vet. J.* 19: 583-595.

Mrudula, V., George, V.T., Balachandran, C. and Murali Manohar, B. 2005. Haematobiochemical ,urinalysis and urinary enzyme alterations in canine nephritis. *Indian Vet.J.*82:826-829

Muraly,P. 2001. *Investigations on etiopathology of vomiting in dogs*.M.V.Sc.Thesis submitted to the Kerala Agricultural University,Trichur.p105

Neer, T.M. 1988. Clinical pharmacologic features of fluroquinolone antimicrobial drugs. *J.Am.Vet.Med.Assoc.* 193: 577-580

Nicolle,A.P., Chetboul, V.,Allerheiligen,T.,Pouchelon,J.L.,Gouni,V.,Vetzel,D.T., Sampedrano,C.C., and Lefebvre,H.P.2007. Azotemia and Glomerular Filtration Rate in Dogs with Chronic Valvular Disease. *J. Vet. Intern. Med.* ;21:943–949

Nyland, T.G. 1995.Ultrasonography of the urinary tract and adrenal glands. *Veterinary Diagnostic Ultrasound.* 1st ed. Nyland,T.G. and Mattoon,J.S.(Eds).W.B.Saunders,Philadelphia.pp30-42

Oglive, G.K. 1993. Prevalence of nephrotoxicosis associated with a four hour saline solution diuresis protocol for the administration of cisplatin to dogs with naturally developing neoplasm. *J.Am.Vet.Med.Assoc.* 202: 1845-1849

Oser, B.L. 1971.*Hawk's Physiological Chemistry.*14th ed.Tata McGraw Hill publishing Ltd.,New Delhi.pp1139-1142

Plevraki, K., Koutinas, A.F., Kaldrymidou, H., Roumpies, N., Papazoglou, L.G., Savvas, I. and Leondides, L. Effects of allopurinol treatment on the progression of chronic nephritis in canine leishmaniosis (*Leishmania infantum*) *J. Vet. Intern. Med.* 20:228–233

Polzin, D.J. 1990. The effects of aging on the canine urinary tract. *Vet. Med.* 5: 472-482.

Polzin, D.J.,Osborne,C.A. and Ross.S 2005. Chronic kidney disease. In: *Text Book of Veterinary Internal Medicine Diseases of the dog and cat.* 6th ed. Ettinger, S.J.and Feldman,E.C.(Eds) Elsevier Saunders, Philadelphia.p. 1991

Pomianowski, A., Lew, S., Kuleta, Z., Snarska, A. and Asprowicz, A.2008. Peritoneal dialysis in a dog with acute renal failure caused by the infection with *Babesia canis. Pol.J.Natur.Sc.* 23(1):257-267.

Ponnuswamy,K.K.,Prathaban,S.and Dhanapalan,P.2009.Nephrosonographic evaluation of renal diseases in dogs.*Indian.Vet.J.*85:421-422

Porzio,P.,Render,J.A. and Baptiste,K.E. 1997.Exertional rhabdomyolysis in an adult Siberian husky.*J.Vet.Emerg.Crit.Care.*7:43-48

Pressler, B.M. and Vaden, S.L. 2003. Managing renal amyloidosis in dogs and cats. *Vet. Med.* 4: 320-333

Puig, J., Vilafranca, M., Font, A., Closa, J., Pumarola, M. and Mascort, J. 1995.Acute intrinsic renal failure and blood coagulation disorders after a snakebite in a dog. *J. Small Anim. Pract.* 36: 333-336

Qari, F.A.2009. Severe rhabdomyolysis and acute renal failure secondary to use of simvastatin in undiagnosed hypothyroidism.*Saudi.J.Kidney.Dis.Transplant*.20:127-129.

Raila, J., Aupperle, H., Raila, G., Schoon, H.A., Schweigert, F.J. 2007.Renal pathology and urinary protein excretion in a 14 month old Bernes mountain dog with chronic renal failure.*J.Vet.Med.*54:131-135.

Randolph, J.F., Scarlett, J., Stokol, T. and MacLeod, J.N. 2004. Clinical efficacy and safety of recombinant canine erythropoietin in dogs with anemia of chronic renal failure and dogs with recombinant human erythropoietin-induced red cell aplasia *J. Vet. Intern. Med.*18:81–91

Reine, N.J. and Langston, C.E.2005. Urinalysis interpretation: How to squeeze out the maximum information from a small sample.*Clin.Tech.Small.Anim.Pract*.20:2-10.

Reusch, C., Vochezer, R. and Weschta, E.1991.Enzyme activities of urinary alanine aminopeptidase and N-acetyl-β-D-glucosaminidase (NAG) in healthy dogs.*J.vet.Med.Assoc*.38:90-98.

Reusch, C.E., Tomsa, K., Zimmer, C., Hoerauf, A., Nett, C., Unterer, S., Glaus, T.M., Schlittner,E. and Pospischil, A.2000.Ultrasonography of the parathyroid glands as an aid in differentiation of acute and chronic renal failure in dogs. *J.Am.Vet.Med.Assoc*.217(12):1849-1852.

Rivers, B.J., Walter, P.A., O'Brien, T.D., King, V.L. and Polzin, D.J. 1996. Evaluation of urine γ-glutamyl transpeptidase-to-creatinine ratio as a diagnostic tool in an experimental model of aminoglycoside-induced acute renal failure in the dog. *J.Am.Anim.Hosp.Assoc*.32(4):323-336

Rubin, S.I. and LeClerc, S.M. 2001. A step by step approach to managing hypercalaemia. *Vet. Med.* 6: 446-475.

Satake,K., Kanazawa,G., Hiura,A., Nishiwaki,H., Ha,S.S., Chung,Y.S., Umeyama,K. and Yukimura,T. 1991.Jpn.J.Surg.21:88-95

Sato, R., Soeta, S., Miyazaki, M., Syuto, B., Sato, J., Miyake, Y., Yasuda, Okada, K. and Naito,Y.2002. Clinical availability of urinary n-acetyl-β-d-glucosaminidase index in dogs with urinary diseases. *J.Vet.Med.Sci.* 64(4):361-365.

Schalm, O.W., Jain, N.C. and Corel, E.J. 1975. *Veterinary Haematology.* 3rd ed.Lea and Febiger,Philadelphia.p.647.

Sheehan, D.C. and Hrapchak.B.B.1980.*Theory and Practice of histochemistry.*2nd ed.C.V.Mosby Co. St. Louis, Toronto. pp148-15

*Slot, C.1965.Operation instructions of the reagent kit to estimate serum creatinine. *Scand.J.Clin.Lab.Invest.* 17:381

Snedecor,G.W. and Cochran, W.G. (1994). *Statistical Methods.* 8th ed. Iowa state University press,Ames,Iowa.

Takahashi, M., Morita, T., Sawada, M., Uemura, T., Harunal, A. and Shimada, A. 2005. Glomerulo cystic kidney in a domestic dog. *J. Comp. Path.* 133, 205-208.

Tietz, N.W. 1986.*Fundamentals of Clinical Chemistry.* W.B.Saunders Co., Philadelphia. p 885.

Toutain, P.L., Lefebvre, H.P. and Laroute, V.2000.N ew insights on kidney insufficiency on disposition of angiotensin converting enzyme inhibitors: case of enalapril and benazepril in dogs.*J.Pharmacol.Exp.Therap.*292:1094-1103.

Triolo, A.J. and Miles, K.G.1995.Renal imaging techniques in dogs and cats.*Vet.Med.*10:959-966.

Uechi, M., Matsuoka, M., Kuwajima, E., Kaneko, T., Yamashita, K., Fukushima, U. and Ishikawa,Y. 2003. The effects of loop diuretics furosemide and torasemide on diuresis in dogs and cats.*J.Vet.Med.Sci.*65(10):1057-1061

Uechi, M., Nogami, Y., Terui, H., Nakayama, T., Ishikawa, R., Wako, Y. and Takahashi, M.1994.Evaluation of urinary enzymes in dogs with early renal disorder.*J.Vet.Med.Sci.*56:555-556.

Vaden,S.L., Levin,J. and Breitschwerdt,E.B.1997.A retrospective case control of acute renal failure in 99 dogs.*J.Vet.Intern.Med.*11(2):58-64

Vaughan,E.D.Jr.,Shenasky,J.H. and Gillenwater, J.Y.1971.Mechanism of acute haemodynamic response to ureteral obstructions.*Invest.Urol.*9:109-112

Velthuysen,M.L.F. and Florquin,S.2000.Glomerulopathy associated with parasitic infections.*Clin.Microbiol.Rev.*13:55-66

Voros, K., Wladar, S., Vrabely, T. and Fenyves.B. 1993. Ultrasonographic diagnosis of urinary bladder calculi in dogs. *Canine.Pract.*18:29-33

Walter, P.A., Feeney, D.A., Johnston , G.R. and O'Leary, T.P. 1987.Ultrasonographic Evaluation of Renal Parenchymal Diseases in the Dog: 32 cases (1981-1986). *J. Am. Vet. Med. Assoc.* 191:999-1007.

Ward, J.P.1976. Urinary γ-glutamyl transpeptidase, an indicator of renal ischaemic injury and homograft rejection. *Br.J.Urol.* 47:765-770.

Widmer, R.W., Biller, D.S. and Adams, L.G.2004.Ultrasonography of the urinary tract in small animals. *J.Am.Vet.Med.Assoc.*225 (1):46-54.

Williams,.A. and Steiner,J.M.(2005) Canine exocrine pancreatic disease. *Textbook of veterinary internal medicine. Diseases of the dog and cat.*6th ed. Ettinger, S.J. and Feldman,E.C.(Eds)Elsevier Saunders. St.Louis, Missouri. p. 1991

Winter,H. and Majid,N.H.1984.Glomerulonephritis-An emerging disease?.*Vet.Bulletin.*54:327-333

Worwag,S. and Langston,C.E. 2008. Acute intrinsic renal failure in cats:32 cases(1997-2004)

*Originals not consulted

Appendix

ANNEXURE – I

PROFORMA

Case No. / Sl No. **Date**

1. Name And Address Of The Owner :
2. Detatils Of The Animal :
Breed :
Age :
Sex :
Colour :
If vaccinated :
If yes, Details :

3. Clinical History

Date	Diseases encountered in the past	Treatment adopted

1. General Clinical Examination :

2.Systemwise Examination :

Urinary system :

4. Clinical Observation

a) Clinical Data

1. Respiration rate (per minute) :
2. Pulse (rate per minute) :
3. Temperature :
4. Mucous membrane : (pale/congested/icteric)
5. Lymph nodes :

b) Clinical Signs

(Present / Absent)

1. Lethargy :
2. Vomiting :
3. Anorexia :
4. Haemoglobinuria :
5. Oedema of any part if any :
6. Ascites :
7. Jaundice :
8. Cough :
9. Dyspnoea :
10. Syncope :
11. Muscle weakness :
12. Exercise intolerance :

5. Results of Special Examination

1. Ultrasonography Findings

Kidney

2. Haemato-biochemical Findings :

Sl no	Parameters	Result	
		Day 1	Day7
1.	Hb (gm/dl)		
2.	RBC (10^6/cu.mm)		
3.	VPRC %		
4.	ESR mm		
5.	TLC(10^3/cu.mm)		
6.	DLC		
	Neutrophils(%)		
	Lymphocytes(%)		
	Eosnophils(%)		
	Monocytes(%)		
	Basophils(%)		
7.	Platelet count		
	Serum Analysis		
	Total Protein(g/dl)		
	Albumin(g/dl)		
	A:G Ratio		
	Serum Creatinine (mg %)		
	BUN (mg%)		
	Gamma GT		
	Potassium		

3. Urinalysis

Physical examination
Protein : Creatinine ratio
Sediments
C&S

6. Diagnosis

7. Treatment

8. Histopathologic observations if any

CLINICO-BIOCHEMICAL AND ULTRASONOGRAPHIC EVALUATION OF RENAL FAILURE IN DOGS

KANARAN P. P.

Abstract of the thesis submitted in partial fulfillment of the requirement for the degree of

Master of Veterinary Science

Faculty of Veterinary and Animal Sciences
Kerala Agricultural University, Thrissur

2009

Department of Clinical Veterinary Medicine
COLLEGE OF VETERINARY AND ANIMAL SCIENCES
MANNUTHY, THRISSUR-680651
KERALA, INDIA

Abstract

The study on "clinico-biochemical and ultrasonographic evaluation of renal failure in dogs" was conducted on 23 dogs.

The parameters studied were signalment, history and clinical signs, physical examination findings, ultrasonography of the kidney, haematology, serum biochemistry and urinalysis, urine protein creatinine ratio, urinary enzymes as markers of renal disease, response to treatment, peritoneal dialysis as a treatment option and postmortem examination and histopathology.

All the renal failure cases studied were associated with nephrotoxic drugs, microfilariosis, pyometra, prostatic enlargement, pancreatitis, rhabdomyolysis or leptospirosis. The cases were divided into renal failure following exposure to nephrotoxic drugs, microfilariosis, pyometra, prostatic enlargement, pancreatitis, rhabdomyolysis or leptospirosis.

The haematological and biochemical values of the diseased animals varied from that of normal animals and did not show any significant difference with the values measured after seven days of treatment indicating that it was not effective. The most common ultrasonographic pattern was hyperechoic kidneys with lack of corticomedullary distinction indicating fibrotic changes in kidney which was confirmed by postmortem examination and histopathology. Estimation of urinary enzymes NAG, GGT and ALP were done in selected animals. There was a sharp difference between diseased and healthy animals.

It was concluded from this study that for effective treatment and management of canine renal diseases, early diagnosis and treatment is a must and that for achieving this goal ultrasonography and estimation of urinary enzymes can be used as effective tools.