STUDIES ON THERAPEUTIC MANAGEMENT OF RENAL FAILURE IN DOGS

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CERTIFICATE

This is to certify that the thesis entitled "Studies on Therapeutic Management of Renal Failure in Dogs" submitted by Mr. Somesh Atmaram Sawale, I.D. No. MVHK-1237 in partial fulfilment of the requirements for the award of MASTER OF VETERINARY SCIENCE in VETERINARY MEDICINE of the Karnataka Veterinary, Animal & Fisheries Sciences University, Bidar is a record of bonafide research work carried out by him, during the period of his study in this University under my guidance and supervision and the thesis has not previously formed the basis for the award of any degree, diploma, associate ship, fellowship or other similar titles.

BANGALORE
MARCH, 2015

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Affectionately Dedicated to

My Beloved Parents

& My Guide

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LIST OF ABBREVIATIONS

%	Per cent
G	Gram(s)
µl	Microlitre
ml	Millilitre
mg	Milligram
kg	kilogram
dl	Decilitre
bid	bis in die
MHz	Mega Hertz
IV	Intravenous
SQ	Subcutaneous
SE	Standard error
EDTA	Ethylene Diamine Tetraacetic Acid
Hb	Hemoglobin
PCV	Packed Cell Volume
TLC	Total Leukocyte Count
PLT	Platelet
CRT	Creatinine

BUN	Blood Urea Nitrogen
PU/PD	Polyuria/Polydypsia
CKD	Chronic Kidney Disease
CRF	Chronic Renal Failure
GFR	Glomerular Filtration Rate
USG	Urine Specific Gravity
IRiS	International Renal Interest Society
ESRD	End Stage Renal Disease
ACE	Angiotensin Converting Enzyme
ACEI	Angiotensin Converting Enzyme Inhibitors
KB	Kibow Biotics

Introduction

I. INTRODUCTION

Among the companion animals, dogs have the credit of being man's oldest friend. Both man and dog have been mutually benefited by this relationship. Man provided dogs with food and shelter; in return they served him loyalilty, friendliness and faithfulness. This relationship between them has grown so intimate over the years that man is very much concerned about the well-being of this companion and willing to take all possible steps to reduce their distress and sufferings.

The kidneys are important paired organs in the body which are important to maintain good health and to sustain life. Kidney is a complex organ and regulates essential homeostatic functions such as excretion of waste products of metabolism, maintenance of a constant extracellular environment through conservation and excretion of water and electrolytes, production of the hormones erythropoietin and rennin which regulate haematopoiesis, blood pressure and sodium resorption; metabolism of vitamin D to its active form. Although, kidney constitutes less than one percent of the body weight, they receive 25 per cent of total cardiac output, thus rendering them susceptible to a great amount of blood borne toxicants.

The number of diseases affecting the kidneys of dogs have increased considerably over the years with acquired diseases being common than congenital defects. In spite of advancement in preventive and trauma medicine, organ failures have become common causes of death in recent years (Defrancesco, 2002). Renal failure is one of the important clinical problems encountered in dogs and is frequent causes of death.

Kidney disease is one of the leading problems that cause considerable morbidity and mortality in dogs. Majority of old dogs suffer some degree of kidney damage thus it is one of the major causes of death in older animals. The underlying cause of the disease might have occurred previously and remained unknown in most cases. The prevalence of renal disease is high in dogs and cats especially in aged population (Polzin *et al.,* 2000). A recent study of general canine population indicated that more than 50 per cent of dogs die or euthanized before 10 years of age and constitutes third most common cause of death in dogs in that age interval (Bonnet *et al.,* 1997).

Renal function tests such as serum creatinine and Blood Urea Nitrogen are indices of glomerular function, since the excretion of creatinine occurs almost entirely by glomerular filtration. The level of BUN and creatinine start to rise only after 75 per cent of nephrons are damaged (Polzin *et al* 2000). Unfortunately, many diseases are not detected until they become generalized leading to serious impairment of renal function. End stage renal failure is associated with a high rate fatality and cost of therapy.

Over the years, many therapeutic and preventive interventions have been developed or advocated for chronic kidney disease in dogs, but evidence of efficacy or effectiveness is often lacking or highly variable.

Conservative medical management of chronic kidney disease (CKD) consists of supportive and symptomatic therapy designed to correct abnormalities in fluid, electrolyte, acid-base, endocrine and nutritional balance. Therapy is designed to minimise the clinical and pathophysiological consequences of reduced kidney function. In general,

this type of management should not be expected to halt, reverse or eliminate renal lesions responsible for CKD.

Therefore, management strategies are most beneficial when combined with specific therapy directed at stabilizing the renal function.

Thus to examine the impact of specific therapy on development of uremic crisis, mortality rate, and progression of renal failure and also to study the efficiency of specific therapy with the conservative therapy in the management of renal failure, the present study is designed with following objectives.

1. Detection of renal failure cases in dogs based on clinical manifestation, hematology, biochemistry, urine analysis and ultrasonography.
2. Renal failure cases will be subjected to conventional and new regimen of treatments.
3. Evaluation of cases, subjected to different regimen of treatments based on clinical signs, hematology, and biochemistry.

Review of Literature

II. REVIEW OF LITURATURE

Review of literature for the present study has been given in this chapter under respective subheadings.

2.1 Incidence:

Dougall *et al.*, (1986) following a study on renal failure in dogs suggested that there was lack of evidence of any predisposition of renal disease related to sex or breed.

Polzin *et al.,* (1989) following a study on chronic renal failure in dogs, opined that the structural and functional changes of the kidney in geriatric animals affects 15 per cent that were 10 years age or older.

There is no age, breed or sex predilection for acute renal failure. Acute renal failure occurs more frequently than is generally recognized and is often misdiagnosed as chronic renal failure (Mary, 1992).

Stanley (1995) reported that renal failure occurs in cats and dogs with comparable frequency, with chronic renal failure being more common than acute renal failure.

David *et al*., (1995) reported that chronic renal failure is the most common form of renal failure in dogs, although commonly considered as the disease of older animals, CRF occurs with varying frequency in dogs of all ages.

Shelly *et al.,* (1997) in a study on dogs with renal failure recorded that the age of ARF patients ranged from 11 months to 15 years. Age of CRF patients ranged from 6 months to 16 years.

The incidence of renal failure in the general population of dogs and cats is 0.5 to 1.5 per cent and 1 to 3 per cent respectively (Brown, 2007).

The prevalence of kidney disease has been estimated to range between 0.5% and 7% in dogs and between 1.6% and 20% in cats (Watson, 2001).

Kavitha (2010) in one study conducted at Veterinary College Hospital, Bangalore observed that occurrence of renal failure in different breeds of dogs ranged from 3.22 to 22.58 per cent. The incidence was highest in the GSD and Non- descript (22.58%) followed by Labrador Retriever (19.35%), Pomeranian (19.35), Dachshund (6.45%), Doberman Pinscher (6.45%), and Dalmatian (3.2%).

2.2 Diagnosis:

Recognizing kidney disease requires consideration of evidence from multiple sources, including renal function tests, serum electrolyte concentrations and acid-base status, urinalysis, and renal imaging studies. Kidney disease is usually suspected on the basis of reduced kidney function or markers of kidney disease. Markers of kidney disease may be recognized from hematologic or serum biochemical evaluations, urinalysis, or imaging or pathology studies. Findings suggestive of kidney disease may also be found by physical examination or from the medical history (e.g. changes in kidney size or shape, changes in urine volume).

According to Brown (2007), the diagnostic tests that are routinely used to establish a diagnosis in a patient with renal failure included urinalysis, urine culture, urine protein to creatinine ratio, serum biochemical panel, complete blood count and

sequential evaluation of serum creatinine concentration and these are useful in assessing the rate of change of renal function over time

Ross (2008) stated that a history of signs such as polyuria, polydipsia, weight loss, selective appetite, deteriorating haircoat occurring over several months is a strong evidence of renal failure.

2.2.1 History and Physical Examination:

Uraemia develops when disturbances in tubular and endocrine functions of the kidneys cause retention of toxic metabolites, changes in the volume and composition of the body fluids, and an excess or deficiency of various hormones (Bergstrom *et al*., 1978).

Robinson *et al.*, (1989) in their work on chronic renal failure reported that the common presenting signs were anorexia (80%), polydipsia (67%), vomition (67%), lethargy (53%), polyuria (33%), and weight loss (33%). Physical findings included dehydration (40%), lumbar and abdominal pain (33%), oral ulceration (20%) and pale mucous membrane (7%).

Raskin, (1995) mentioned that uremic encephalopathy may accompany acute or chronic renal failure, but in patients with acute renal failure the symptoms are more pronounced and progression of disease is more rapid.

According to Nagode *et al*., (1996) although secondary renal hyperparathyroidism and renal osteodystrophy are well known sequel of chronic renal failure, clinically important renal osteodystrophy is rarely seen in dogs and cats.

Metabolic acidosis is a well-known sign of CRF, resulting primarily from the limited capacity of damaged kidneys to excrete hydrogen ions and secondarily, from disturbed ammonia genesis, reduced filtration of phosphates and sulphates, the loss of bicarbonates and the reduced secretion of protons from renal tubules (Kimmel, 1998).

Polzin *et al.*, (2000) stated that upto 67 per cent loss of renal function occurs as clinically asymptomatic condition and that with a 67-75 per cent of loss of renal function polyuria and polydipsia may be manifested and they further stated that loss of 75-95 per cent of renal function would be manifested as vomiting, diarrhoea, apathy and when less than 10 per cent of renal function is present, it was accompanied with signs of uremic encephalopathy, indicating terminal stages of illness.

Pugliese *et al.*, (2005) stated that with a loss of 67-75 per cent of the filtration rate, severe polydipsia and polyuria occurred; when renal failure increased (75-90%) the accumulation of blood nitrogen catabolic products determined the occurrence of systemic signs such as anorexia, weight loss and specific signs such as vomiting and diarrhoea. When the residual renal function was found to be less than 10 per cent uremia was present associated with the neurological signs (uremic encephalopathy) that indicated terminal stage of illness.

Reine and Langston (2005) stated that the presence of isosthenuria might be suggestive of primary renal failure with renal disease. Isosthenuria occurs with greater than 66 per cent damage to the kidney (renal insufficiency) where as azotemia occurs after more than 75 per cent renal damage has been sustained (renal failure).

Robertson and Seguin (2006) opined that many cases of chronic renal failure are asymptomatic (other than PU/PD) until dehydration leads to decompensation, leading to more acute history from the owner perspective.

According to Mcgrotty (2008) clinical signs of chronic renal failure can be variable and depends upon the stage of renal disease but may include polyuria and polydipsia, decreased appetite, weight loss and depression.

Grauer (2009) stated that decreased production of erythropoietin contributes to the non-regenerative anaemia of CKD and decreased metabolism and excretion of parathyroid hormone and gastrin contribute to osteodystrophy and gastritis respectively.

According to Ross (2011) common clinical manifestation of uremia include gastrointestinal signs, anemia, coagulopathy, acidosis, hyperkalaemia, calcium and phosphorus derangements, endocrine abnormalities, malnutrition and cardiovascular complications.

Pradhan and Roy (2012) in their study on chronic renal failure in dogs found that dogs which are in advanced stage of renal failure showed nervous signs like ataxia, tremors, incoordination, seizures, syncope and progressive deterioration of health.

2.2.2 Haematology:

King *et al.,* (1992) reported non regenerative normochromic normocytic anemia in 70.6 per cent of dogs with chronic renal failure and were of opinion that many factors including decreased erythropoietin, haemolysis and blood loss might influence the development of anaemia in CRF.

Lulich *et al.,* (1992) stated that erythropoietin is produced primarily in the peritubular interstitial cells of the inner renal cortex and outer medulla in the kidney, and as kidney disease progresses, there are fewer erythropoietin-producing cells within the kidneys.

Erslev and Besarab, (1995) in their study on renal failure, observed that uraemia had been associated with decreased RBC survival, but the pathophysiology of that was unclear and most likely multifactorial.

Chronic renal failure could be associated with lymphopenia, which reflected the effects of endogenous glucocorticoids or stress of chronic disease (Robertson and Seguin, 2006).

Rusenov *et al.,* (2009) observed severe erythropenia and hypochromia in dogs with CRF and stated that the main cause for hypo proliferative anaemia in animals with CRF was erythropoietin deficiency.

Chalhoub *et al.,* (2011) mentioned that acute and chronic inflammation contributed to anemia of renal disease by the production of inflammatory cytokines and substances such as hepcidin that will decrease erythropoietin function, red cell survival and available iron.

Bradea *et al.,* (2013) concluded that complete blood count in CKD provided useful information about the progress of the disease as well as appreciation of type of anemia offering additional information for therapeutic protocol adjustment for amending

induced hematological consequences. Nonregenerative anemia represented a common finding in chronic kidney disease pathology in dogs.

2.2.3 Creatinine and BUN:

Creatinine is a substance that the body produces during normal metabolism. The body eliminates creatinine almost exclusively through the kidneys' filtration process, so measurement of creatinine is an accurate estimation of how well the kidney filtration processes are working. Anything that alters the ability of the kidneys to filter efficiently (such as dehydration) can cause changes in the level of creatinine in the blood. The BUN is a measurement that represents the level of urea in the blood. Urea is considered one of the body's waste products. It is produced when the liver participates in protein metabolism, and it is usually eliminated from the body by the kidneys. Therefore, both the liver and kidneys must function properly for the body to maintain a normal level of urea in the blood (Wyss & Kaddurah-Daouk, 2000).

Gabrish (1973) reported that creatinine was a more reliable diagnostic tool compared to that of serum urea.

Brown *et al.,* (1998) stated that azotemia is the presence of elevated serum concentrations of blood urea nitrogen (BUN) and creatinine and further observed that chronic renal failure (CRF) the presence of azotemia of renal origin for a minimum duration of 2 weeks.

Finco *et al*., (1999) stated that clinically, plasma creatinine concentration was commonly measured to assess renal function as a crude estimate of GFR.

International Renal Interest Society (IRiS) proposed the staging system for canine chronic kidney disease. Staging is based on the plasma creatinine level as the major determinate for four stages.

Stage	Creatinine
I	< 1.4 mg/dl
II	1.4-2.0
III	2.0-5.0
IV	>5.0 (IRiS).

Plasma creatinine and urea levels are typically used as biochemical markers of kidney disease (Mcgrotty, 2008).

Arulmozhi *et al*., (2010) found systemic uremia and encephalopathy in the dogs with progressive unresponsive renal failure. The haemogram showed anemia and blood biochemistry revealed severe uremia with 276 mg/dl urea nitrogen and 18.2 mg/dl serum creatinine.

Kavitha (2010) in a study conducted on early diagnosis of renal failure in dogs stated that the creatinine and BUN values were studied to assess the kidney function, since these are used as standard tests. The creatinine and BUN values of less than 1.4 mg/dl and less than 30 mg/dl respectively were considered normal. The normal levels of creatinine and BUN in blood are indicators of ability to eliminate nitrogenous waste products successfully.

According to Polzin (2011) the relationship between serum creatinine and glomerular filtration rate (GFR) is such that every time GFR declines by half, the serum creatinine concentration doubles.

Lefebvre (2011) stated that plasma creatinine concentration is currently considered as the best indirect marker of GFR and is also used by the International Renal Interest Society (IRiS) to stage canine and feline chronic kidney disease.

2.2.4 Urine Specific Gravity

English (1973) stated that measurement of urine specific gravity and osmolality are used to determine the kidneys ability to concentrate urine. The ability to concentrate urine in the chronically diseased kidney depends upon adequate secretion of antidiuretic hormone and the presence of enough nephrons.

Carl *et al.,* (1995) reported that, dogs with primary renal failure, azotemia usually follows loss of ability to concentrate urine to a specific gravity of at least 1.030.

The specific gravity cannot be taken as an early indicator of renal damage as the kidneys have a tremendous reserve capacity. Impairment of the kidneys ability to concentrate or dilute urine may not be detected until at least two third of the total population of nephrons has been damaged (Osborne *et al*., 1995).

According to Haller (2002) determination of USG was very important in assessment of renal disease. It should always be measured before any treatment is initiated because fluids, glucocorticoids or diuretics may result in artificially diluted urine. Hyposthenuric urine (1.001-1.007) indicated active dilution, isosthenuria (1.007-

1.015) indicated unchanged excretion and hypersthenuric urine indicates active concentration of the glomerular filtrate.

Reine and Langston (2005) stated that the presence of isosthenuria (USG 1.007 to 1.012) might be suggestive of primary renal failure with renal disease. Isosthenuria occurs with greater than 66 per cent damage to the kidneys where as azotemia does not occur until >75 per cent damage has been sustained.

2.2.5 Ultrasonography:

Ultrasound examination is an integral tool in the thorough evaluation of the urinary system. Ultrasound is a non-invasive, non painful and economical procedure that provides valuable information concerning morphology, vascular status and luminal contents usually with little or no sedation.

Cartee *et al*., (1980) worked on the usefulness of ultrasonography in the diagnosis of renal diseases and found to be useful in diagnosis of hydronephrosis, renal calculi, and renal neoplasia.

Vaden *et al*., (1998) reported that the ultrasonography can be used to characterize the renal shape and size. It provided information about renal parenchyma, increased overall renal echogenicity and decreased corticomedullary distinction can be seen but this can not be diagnostic for CRF.

Churchill *et al*., (1999) stated that, in normal sonographic anatomy of kidney the cortex is outer rim of tissue and is normally hyperechoic to the more central hypoechoic

medulla. The cortex is typically isoechoic to hypoechoic to the liver and hypoechoic to the spleen.

Tripathi and Mehta (2010) diagnosed renal failure in 7 dogs out of 72 dogs. Out of that 4 dogs showed ultrasonographyically loss of architectural detail of renal parenchyma, indistinct contours of renal cortex, hyperechoic periphery and small sized kidneys, lack of demarcation of corticomedullary junction and rest 3 dogs showed small sized kidneys, loss of architectural detail of renal parenchyma with well-defined irregular border in ultrasonography.

Satish *et al*., (2012) conducted the ultrasonography of urinary system in ten dogs, and found that both the kidneys were of equal size and the left kidney was sonographically easily detectable in comparison to the right kidney.

2.3 Treatment:

A clinical action plan should be developed for each patient based on the diagnosis, stage of renal failure, existing complications and co-morbid conditions, and risk factors for progression of kidneys. In general treatment of renal failure includes 1) specific therapy, 2) prevention and treatment of complications of decreased kidney function (conservative medical management), 3) management of co-morbid conditions, and 4) therapy designed to slow loss of kidney function.

Renal diets appear to reduce the magnitude of proteinuria in protienuric dogs and are advocated for all dogs with proteinuric kidney disease (Burkholder, 2004).

Ross *et al.,* (2006) studied the effectiveness of diet therapy in stage 2 and stage 3 renal failure dogs and they found that the risk of developing uremic crisis was reduced by approximately 75 per cent for dogs consuming the renal diet as compared to dogs consuming an adult maintenance diet.

Kavitha *et al.,* (2013) in their study in 102 dogs based on chronic renal failure concluded that nearly fifty per cent of dogs were in stage I, II, III of renal failure, where pharmacological strategies could be employed to delay the progression of the disease.

2.3.1 Conservative Medical Management:

According to Polzin *et al.,* (1984) it is necessary to emphasize that the reduction of protein ingestion is a fundamental step when the critical level of renal function is reached. The reduction in intake of non-essential dietary proteins should decrease the quantity of protein metabolic products, limiting the effects of uremic toxins and improving the nutritional status of the patient. Such protein restriction should not modify food palatability and it should not induce a negative balance of proteins as this causes loss of muscular protein and very severe clinical condition.

Michell *et al.,* (1989) mentioned that a rough estimate of volume replacement may be made from the PCV alone. A common formula, assuming the extracellular deficit was to allow 10 ml/kg body weight for each one percent rise in PCV above normal level.

Jacob *et al.,* (2002) in a study in 38 dogs with spontaneous chronic renal failure used the H2 blockers and metoclopramide orally in those dogs which were suffering from vomiting and persistent anorexia.

Chronic administration of subcutaneous balanced electrolyte solutions has been advocated to prevent dehydration, maintain renal blood flow and GFR, increase urine output and ameliorate clinical manifestation of uraemia (Adams, 2004).

According to Brown (2007) hypokalemia is frequent in some cases of renal failure; in fact, muscle weakness may be the principle presenting sign; in these cases, much higher doses of potassium as shown below may be needed:

Serum Potassium	IV/SQ Supplementation (mEq/250 ml)
3.0-3.5	5/10
2.5-3.0	7/14
2.0-2.5	10/20
<2.0	12/24.

According to Polzin (2009) treatment of uremic gastritis includes; use of H2 blockers (ranitidine, famotidine) to limit the gastric acidity, use of antiemetic's (metoclopramide) to suppress the nausea and vomiting, and use of sucralfate for providing mucosal protection.

Maddison (2010) stated that fluid therapy is an essential component of the management of chronic kidney disease and the fluid rates should be approximately twice that of normal of maintenance rates. The fluid required for maintenance is approximately equal to 50 ml/kg/day.

Conservative medical management of chronic renal failure consists of supportive and symptomatic therapy designed to correct deficits and excess in fluids, electrolyte, acid base, endocrine, and nutritional balance thereby minimizing the clinical and pathophysiological consequences of reduced renal function (Roudebush *et al.*, 2010).

2.3.2 Probiotic Therapy:

Probiotics are live microorganisms which when administered in adequate amounts confer a health benefit on the host. Prebiotics are short-chain or long-chain oligosaccharides that are not digestible by mammalian digestive enzymes but are fermented in the colon by microorganisms.

A combination of three bacterial strains (*Lactobacillus acidophilus KB31, Streptococcus thermophilus KB27 and Bifidobacterium longum KB35*) appears promising and finds potential application as a dietary supplement, decreasing concentrations of nitrogen containing metabolites and helps to maintain healthy kidney function (Friedman *et al*., 2001).

Dotan and Rachmilewitz (2005) stated that probiotics administered to clinically ill patients should originate in the species being treated and should be non-pathogenic, resistant to digestion by gastric acid and intestinal enzymes, able to adhere to the intestinal epithelium, and capable of influencing host immune responses.

Palmquist (2006) stated that the use of a mixture of probiotic bacteria (*Streptophilus thermophilus, Lactobacillus acidophilus and Bifidobacterium longum*) orally is effective

in reducing feline azotemia and these bacteria have an affinity for many uremic toxins. Results indicated a decrease in creatinine levels in six out of seven patients treated (86%).

According to Wynn (2009) uremic toxins diffuse passively from the blood into the lumen of gastrointestinal tract. Urease producing probiotic species hydrolyse urea and maintain a concentration gradient that favours diffusion of urea from the blood to the gastrointestinal tract lumen.

Ranganathan *et al.,* (2009) concluded in a study based on chronic kidney disease (CKD) in human patients that oral ingestion of a probiotic bacterial regimen in patients with CKD was well tolerated, with decrease in blood urea nitrogen (BUN) and uric acid, possibly contributing to an improved quality of life.

Probiotic supplementation may alter the microbiota in the gut and will likely increase saccharolytic activity and promote increased amounts of beneficial by-products for the host. Increased saccharolytic activity may also decrease proteolytic activity, thus decreasing production of protein-bound uremic solutes and intestinal inflammation (Zirker, 2014).

2.3.3 Punarnawadi Mandur

The whole plant of *Boerhaavia diffusa* is a very useful source of the drug *punarnava*, which is documented in Indian Pharmacopoeia as a diuretic and was used in the treatment of nephritic syndrome and urinary disorders in human patients (Singh and Udupa, 1972).

Singh *et al.*, (1991) stated that Punarnava (*Boerhaavia diffusa*) an ayurvedic medicine showed equivalent diuretic effect to furosemide. *Boerhaavia diffusa* increases the protein level and reduces the urinary protein excretion. It is a clinically useful and safe drug in nephrotic syndrome.

Boerhaavia diffusa Linn., a herbaceous member of family *Nyctaginaceae*, is also known as Punarnava, Raktapunarnava, Shothaghni, Kathillaka, Kshudra, Varshabhu, Raktapushpa, Varshaketu amd Shilatika in India (Yelne *et al*., 2000).

Sathyapriya *et al*., (2009) in a study on antioxidant status in polycystic end stage renal disease (ESRD) in human patients, observed that chronic renal failure (CRF) induces the anemia by shortening the life span of erythrocytes, due to an increase in oxidative stress, which is considered to be one of the major risk factors in the CRF patients and use of aqueous extract of *B. diffusa* showed a significant antihemolytic activity on the erythrocytes of the polycystic ESRD patients.

According to Pareta *et al*., (2010) *Boerhaavia diffusa* Linn. is a plant widely used in India, as a traditional medicine for the treatment of renal disorders including urolithiasis as mentioned in Ayurveda, Charaka Samhita, and Sushrita Samhita.

Surendra *et al.*, (2011) stated that due to the combination of diuretic, antioxidants and antinflammatory activities of *Boerhaavia diffusa* is regarded as therapeutically highly efficacious for the treatment of inflammatory renal disease, nephrotic syndrome, oedema and ascites.

Rajpoot and Mishra (2011) stated that *Punarnava* is regarded therapeutically highly efficacious for the treatment of renal inflammatory diseases and common clinical problems such as nephritic syndrome, oedema, and ascites developing at the early onset of the liver cirrhosis and chronic peritonitis.

Pradhan and Roy (2012) based on their studies on chronic renal failure in dogs concluded that treatment with calcitriol, sucralfate and sharkoferrol are useful in the treatment of renal failure in dogs along with the herbal therapy of Nephtone.

Mohana Lakshmi *et al.,* (2012) stated that medicinal plants may serve as a vital source of potentially useful new compounds for the development of effective therapy to combat a variety of kidney problems and elucidated the list of nephroprotective medicinal plants which are scientifically proved in treating renal disorders including *Boerhaavia diffusa*.

Bhowmik *et al.,* (2012) mentioned that *Punarnava* has been reported to increase serum protein level and reduce urinary protein excretion in clinical trials in human patients suffering with nephritic syndrome.

Mahesh *et al*., (2012) stated that *Boerhavia diffusa* extracts possessed significant levels of enzymatic and non-enzymatic antioxidants. The results of the enzymatic and non-enzymatic antioxidants in *Boerhavia diffusa* indicated that they possess preventive and productive role to maintain the cell survival, cellular interaction and maintenance of cell membrane architecture.

2.3.4 Rubenal

Rhubarb has been used for a variety of conditions, including cancer, GI problems, hyperlipidemia and renal disease. Most of the research into Rhubarb's clinical benefits has been conducted in China. Studies into the effects of Rhubarb on both clinical and experimentally induced renal disease have found benefits in slowing the progression of chronic renal disease, effects similar to those found with angiotensin-converting enzyme inhibitors such as captopril and enalapril. Rhubarb has also been found to reduce renal fibrosis. Improvements in creatinine, proteinuria have also been consistently demonstrated.

Rheum palmatum (Rhubarb) root originates from china and is now cultivated around the world, the cooked root, which decreases anthraquinone levels and thus reduces the cathartic nature of plant, and has long been used as a kidney tonic (Natori *et al*., 1981).

In a human clinical trial, 151 chronic renal failure patients with elevated serum creatinine levels were divided into 3 groups. One group received rhubarb extract, another group received captopril, an ACE inhibitor, another group received both treatments. All patients were given a low protein and low phosphorus diet. Follow up over an average of 32.5 months found a significant reduction in symptoms of uremic nausea and anorexia. The frequency of end stage renal failure was 54.3 per cent for the ACE inhibitor group, 25.9 per cent for the Rhubarb treated group, and 13.1 per cent for the rhubarb and ACEI group (Yu *et al*., 1995).

Li (1996) in clinical studies on the effects of rhubarb in patients with chronic kidney disease reported that rhubarb was able to reduce proteinuria and improve renal function by itself and might also cause further reduction of proteinuria and improvement in renal function when used together with angiotensin converting enzyme inhibitors.

Sanada (1996) conducted clinical trials using rhubarb root extracts in patients with chronic kidney disease in 38 patients and reported that 1 gm rhubarb per day maintained serum creatinine levels compared to rising levels seen in controls not treated with rhubarb.

Zang and Nahas (1996) examined the effect of rhubarb extract on the development of renal failure in wistar rats. Rhubarb extract treatment decreased proteinuria and glomerulosclerosis as compared to the rats with no treatments.

Hadjzadeh *et al*., (2013) in their study on effect of aqueous extract of Rheum ribes on cisplatin induced nephrotoxicity in rats, found that daily administration of 150 mg/kg aqueous extract of Rheum ribes had little effect on biochemical parameters in this dose. This may have been partially due to its time course action on biochemical parameters.

Zhong *et al.,* (2013) in their study on lab animals showed that use of Rheum and its components (emodin, rhein) promotes waste product excretion, reduction in proteinuria, and improvement in renal function. Rheum and Emodin were found to have antioxidant effects in rat acute kidney models.

Materials and Methods

III. MATERIALS AND METHODS

Materials and methods of the present study are presented in this chapter under 3.1 and 3.2 sections.

3.1 Materials:

Materials consisted of animals, clinical samples (blood, serum, urine), chemicals, reagents, glassware, instruments, (refrigerator, water bath, biochemical analyzer, ultrasound machine) and other laboratory materials. The materials that were utilized and the methods followed in the present study are described under the following headings.

3.1.1 Animals:

Dogs with clinical signs suspected for renal failure presented to the veterinary college hospital were selected for the study. A total of 40 dogs were selected for the study based on history, clinical signs, clinical examination, haematology, biochemistry, urinalysis and ultrasonography.

3.1.2 Clinical Materials

3.1.2.1 Blood:

Whole blood from dogs with EDTA and without EDTA for serum separation was collected by cephalic or saphenous venipuncture in vacutainers.

3.1.2.2 Urine:

A spot sample of mid-stream urine was collected into urine collecting vial and were processed either as, as voided or by catheterization into urine collecting vial and were processed.

3.1.3 Laboratory and Other Clinical Materials:

Pipettes, Vacutainers, Sterile vials for urine collection, glass wares like test tubes, refractometer, dispovan syringes 2ml, scalp vein set (18-21G), drip set, infant feeding tubes of different sizes for urine collection were utilized for the present study.

3.1.4 Reagents: Biochemical Test Kits

- BUN kit was procured from Erba Diagnostics, Germany.
- Creatinine kit was procured from Span Diagnostic, Surat, India.

3.1.5 Instruments:

- Ultrasound machine manufactured by General Electronics, New York, United States.
- Semi biochemical analyzer manufactured by Trivitron Health Care, Chennai, India.
- Automatic blood analyzer manufactured by Erma INC. Tokyo.
- Centrifuge machine manufactured by Remi, Cama Industrial Estate, Goregaon East, Maharashtra, India.
- Incubator manufactured by Scientek Services, Bangalore, India.
- Hand held refractometer manufactured by Erma INC, Tokyo, Japan.

3.1.6 Therapeutic Materials:

- Intravenous fluids:
  - Dextrose 5% manufactured by Claris Otsuka Ltd. Ahmedabad.
  - Ringers lactate manufactured by Claris Otsuka Ltd. Ahmedabad.
- Antiemetics: Metoclopramide (Perinorm, marketed by J.B. Chemicals & Pharmaceuticals Ltd. Mumbai).
- H2 blockers: Ranitidine (Rantac, manufactured by Ipca Laboratories Ltd. Mumbai)
- Multivitamin: Vitamin B complex (Bplex, manufactured by Anglo French Drugs & Industries Ltd.).
- Herbal nephroprotectant tablets: Punarnawadi Mandur manufactured by Shree Baidyanath Ayurved Bhavan Pvt.Ltd.
- Probiotics: Azodyl –Manufactured by Vétoquinol USA

Ingredients: Kibow Biotics [*E. thermophiles* (KB 19), *L. acidophilus* (KB 27), *B. longum* (KB 31), Psyllium husk].

- Glomerulo protectant & Antifibrotic: RUBENAL, Manufactured by Vétoquinol USA.

Ingredients**:** **Anthranoids**: Rhein, Emodin, Aloe- emodin, **Tannins**: Gallotannins, Cathechin, Procyanidin stilbene derivatives.

3.2 Methods:

3.2.1 Selection of Animals:

A total of 40 dogs diagnosed as renal failure based on history, clinical signs, hematology, and biochemistry were selected and subjected to different therapeutic regimens. The 40 cases were randomly allotted to four different treatment groups, Group I, II, III and IV each having 10 dogs.

3.2.2 Collection of Sample:

3.2.2.1 Blood

Blood (2ml) was collected in vacutainers with and without EDTA (0.5-2mg/ml of blood) by cephalic or saphenous venipuncture from those animals with clinical signs suggestive of renal failure for evaluation of hematological and biochemical parameters. Whole blood with EDTA was used for estimation of heamatological parameters like TLC, Hb, PCV and Platelet count. Serum was separated and used for estimation of blood biochemical parameters such as creatinine and blood urea nitrogen.

3.2.2.2 Urine

Mid-stream urine was collected from the animals either by catheterization or during natural voiding by proper cleaning of genitalia.

3.2.3 Hematology

Hematological parameters such as Total Leukocyte Count (TLC), Hemoglobin (Hb), Packed Cell Volume (PCV) were analyzed using the automated blood analyzer.

3.2.4 Blood Biochemistry

Serum biochemical parameters such as serum creatinine and Blood Urea Nitrogen (BUN) were analyzed by Aortas Semi Biochemical Analyzer by standard procedures described by the manufacturer using the kits supplied by Erba Diagnostics, Germany.

3.2.5 Urine Analysis

Collected urine was used for estimation Urine Specific Gravity (USG) by using handheld refractrometer.

3.2.6 Ultrasonography

The kidneys were scanned by placing the animals in either lateral or dorsal recumbency by using the ultrasound machine in the Department of Veterinary Medicine Veterinary College, Bangalore. The ultrasound examination of kidneys was done by using the high frequency transducers (7-10 MHz) which provided good penetration and good detail. Ultrasound examination was done to examine the echogenicity of cortex & medulla and to see the corticomedullary distinction.

3.2.7 Groups

Based on the results of serum Creatinine (sCr > 1.4 mg/dl) and hematology (normal WBC count) 40 animals with renal failure were selected and randomly divided into 4 groups Group I, Group II, Group III and Group IV of 10 animals each.

3.2.7. 1. Group I

Animals of Group I received conventional therapy with the intravenous fluids, antiemetic, H2 blockers and multivitamins as per the clinical signs of the animals. The intravenous fluids used were Dextrose 5% and Ringers lactate. The volume of fluids administered was based on the clinical status of animals.

H2 blockers like Rantac @ 1-2 mg/kg and antiemetics like Perinorm @ 0.5 mg/kg were used for those animals with clinical signs of vomition.

Vitamin B complex (Beplex) was used at the dose rate of 1 ml/10 kg of body weight intramuscularly during the whole period of treatment to improve the appetite and quality of life. Treatment was continued for a period of one month.

The various hematological, biochemical parameters were evaluated on zero day, 3^{rd}, 7^{th}, 14^{th}, and 28^{th} day.

3.2.7. 2. Group II

Animals of Group II received conventional therapy along with one specific therapy i.e. Herbal nephroprotectant (Punarnawadi Mandur). The tablets were administered for duration of one month at the dose rate of 1 tablet twice a day for large breeds of dogs (>20 kg) and one tablet once in a day for small and medium breeds of dogs (< 20 kg).

The various hematological, biochemical parameters were evaluated on zero day, 3^{rd}, 7^{th}, 14^{th}, and 28^{th} day.

3.2.7.3 Group III

Animals of Group III received conventional therapy with one specific therapy i.e. probiotic capsules. AZODYL Marketed by: Vetoquinol USA, Inc.

The capsules were administered orally for the duration of one month at the following dose rate:

Weight	Dose
2.3 kg (5lbs)	One capsule
2.3 – 4.5 kg (5-10 lbs)	Two capsules daily (one capsule in the morning and one capsule in the evening).
>4.5 kg (> 10 lbs)	Three capsules daily (two capsules in the morning and one capsule in the evening).

These capsules were given whole and not opened or crushed, allowed free access to fresh drinking water.

The various hematological, biochemical parameters were evaluated on zero day, 3^{rd}, 7^{th}, 14^{th}, and 28^{th} day.

3.2.7.4. Group IV

Animals of Group IV received conventional therapy along with one specific therapy with Rhubarb supplementation (Rubenal), Marketed by: Vétoquinol USA, Inc. These tablets are containing anthranoids like rhein, emodin, aloe-emodin and tannins like gallotannins, cathechin, procyanidin derivatives, and these were administrated orally.

This therapy was continued for duration of one month and dose was based on the weight of the dog.

Weight	**Dose**
8 to 12 kg	Half tablet twice a day.
13 to 25 kg	1 tablet bid.
26 to 45 kg	2 tablets bid.
> 45 kg	3 tablets bid.

The various hematological, biochemical parameters were evaluated on zero day, 3rd, 7th, 14th, and 28th day.

3.2.8 Classification of Renal Failure Cases:

According to International Renal Interest Society (IRiS) standards based on serum Creatinine levels the renal failure cases were classified into four stages.

Serum creatinine (mg/dl)	**Stage of renal failure**	**Azotemia**
<1.4	Stage I	Non azotemic stage
1.4 – 2.0	Stage II	Mild azotemia
2.1 – 5.0	Stage III	Moderate azotemia
>5	Stage IV	Severe azotemia

3.2.9 Statistical Analysis:

Statistical analysis was performed using two way ANOVAs of variance and correlation analysis by using Graph pad prism software.

Results

IV. RESULTS

The results of study are presented in this chapter under respective subheadings.

4.1 Occurrence of Renal Failure

In the present study 40 cases were confirmed as renal failure based on history, clinical signs, physical examination, haematology, blood biochemistry, urine specific gravity and ultrasonography.

4.1.1 Breed-wise Occurrence of Renal Failure:

The occurrence of renal disease in the current study was more in Labrador Retriever (37.5%) followed by Non-descript (27.5 %), German Shepherd (17.5%), Pomeranian(Spitz) (5%), Cocker Spaniel (5%), Great Dane (2.5%), Doberman Pinscher (2.5%), Lhasa Apso (2.5%). The details are shown in the Table 1.

4.1.2 Gender-wise Occurrence of Renal Failure:

The occurrence of renal disease in the present study was more in males (65%) as compared to females (35%). The details are shown in the Table 2.

4.1.3 Age-wise Occurrence of Renal Failure:

The average age of occurrence of renal disease was 8.5 years. The highest incidence of 60% (24/40) was recorded in 5 to 10 years group, followed by 27.5 % (11/40) in 10 to 15 yrs group, 12.5% (5/40) in 1 to 5 yrs group. The details are shown in the Table 3.

4.2 Diagnosis of Renal Failure:

The dogs tentatively diagnosed as renal failure based on based on history, clinical signs, physical examination, hematology, blood biochemistry, urine specific gravity and ultrasonography, were subjected for serum creatinine estimation and those with > 1.4 mg/dl (Stage II) serum creatinine were considered to have renal failure.

4.2.1 History:

On history collection it was found that dogs with renal failure were ill before being presented to the clinic and were categorized into three different time periods. Out of 40 cases of renal failure, eight (20%) dogs were ill for 0 to 5 days, nine (22.5%) were ill for 6 to 10 days and twenty three (57.5%) dogs were ill for more than 10 days. The details are shown in Table 5

In the present study, different food habits were recorded in the renal failure cases. Nineteen (47.5%) dogs were non-vegetarian, twelve (30%) were Veg+Egg and nine (22.5%) dogs were purely vegetarian. The details are shown in Table 6.

4.2.2 Clinical Manifestations Exhibited by Dogs with Renal Failure:

Most common clinical signs recorded were weakness, anorexia, vomiting, weight loss and polyuria /polydypsia.

Among the 40 renal failure dogs, 82.5% of the dogs exhibited weakness followed by 75% anorexia, 55% poor hair coat, 70% weight loss, 65% pale mucus membrane, 62.5% vomition, , 60% polyuria/polydipsia, 37.5% emaciated body condition, 27.5% nervous signs, 20% diarrhoea, 17.5% halitosis, 17.5% oral ulcers and 7.5% congested

mucous membranes. The details of other symptoms exhibited by affected dogs are shown in the Table 4.

4.2.3 Urine Specific Gravity:

Urine in the affected dogs was collected on the zero day of study for analysis of urine specific gravity. The specific gravity of urine in affected dogs ranged from 1.008 to 1.035 with mean of 1.019 ±.0012. Values were categorised in three different ranges. Thirteen animals were having urine specific gravity in the range between 1.007-1.015, twenty three animals were having USG in the range between 1.016 – 1.030 and four animals were having USG values >1.030. Details were shown in the Table 7.

4.2.4 The mean ± SE of Haematological and Biochemical Values on Zero Day:

The mean ± SE values of Total Leukocyte count (TLC/ul), Haematocrit (PCV %), Haemoglobin (Hb gm/dl) and Platelet/ul on zero day were 10998.75 ± 642.70, 34.76 ± 1.49, 10.66 ± 0.43 and 258600 ± 20906.1 respectively. The Total Leukocyte Count and Platelet count were studied to rule out the cases of infectious diseases (Leptospirosis) and Ehrlichiosis. The details are shown in the Table 9.

The mean ± SE values of serum Creatinine (mg/dl) and Blood Urea Nitrogen (mg/dl) on zero day were 6.15 ± 0.67 and 76.90 ± 6.86. The details are shown in the Table 9.

4.2.5 Ultrasonographic Findings in Renal Failure:

Out of 40 cases scanned the findings were “end-stage” kidneys (n = 20), nephritis (n =3), nephrocalcinosis (n =2), and renal cyst (n = 1). The significant

ultrasonographic features in these affections included small kidneys with loss of corticomedullary demarcation ("end-stage" kidneys); increased cortical echogenicity (nephritis) and diffuse, small, multiple hyperechoic structures in the renal parenchyma with distal acoustic shadowing (nephrocalcinosis); small spherical inter cortical anechoic structures fluid (renal cysts). The details are shown in the Table 8.

4.3 Classification of Renal Failure Dogs According to International Renal Interest Society Standards Based on Serum Creatinine Levels (Stage Wise Classification).

Renal failure in canines is classified as per the standards of International Renal Interest Society (IRiS) on the basis of serum creatinine level. In the present study, out of 40 cases 50 per cent of cases were found in Stage III (creatinine 2.1- 5), 50 per cent cases were found in Stage IV (creatinine >5), and no cases were found in Stage I and Stage II. The details are shown in the Table 10.

4.4 Haematological Studies on Renal Failure Dogs.

4.4.1The Mean ± SE Values of Hb (gm/dl) (on zero & 28th day):

The mean ± SE values of Hb of Group I , Group II, Group III and Group IV on zero day were 9.57 ± 0.42, 11.36 ± 0.92, 12.03 ± 0.95 and 9.7 ± 0.93 respectively.

The mean ± SE values of Hb of Group I , Group II, Group III and Group IV on 28th day were 7.27 ± 1.05, 10.62 ± 0.81, 12.16 ± 0.69 and 11.11 ± 1.03 respectively. There was no statistical significant difference between Groups at P>0.05. The details are shown in the Table 11.

4.4.2 The Mean ± SE Values of PCV% (on zero & 28th day):

The mean ± SE values of PCV of Group I , Group II, Group III and Group IV on zero day were 29.69 ± 1.34, 38.1 ± 3.39, 37.06 ± 3.21 and 34.2 ± 3.21 respectively.

The mean ± SE values of PCV of Group I , Group II, Group III and Group IV on 28th day were 23.1 ± 3.94, 34.02 ± 2.04, 37.94 ± 2.46 and 38.96 ± 0.95 respectively. There was no statistical significant difference between the values of any group on respective dates at the $p>0.05$. The details are shown in the Table 12.

4.5 Mean Biochemical Values in Renal Failure Dogs

4.5.1 The Mean ± SE Values of Serum Creatinine (mg/dl) (on zero & 28th day):

The mean ± SE values of creatinine of Group I , Group II, Group III and Group IV on zero day were 6.3 ± 1.27, 7.63 ± 1.89, 5.26 ± 0.86 and 5.01 ± 0.9 respectively.

The mean ± SE values of creatinine of Group I , Group II, Group III and Group IV on 28th day were 5.87 ± 0.18, 3.4 ± 0.74, 2.76 ± 0.32 and 2.13 ± 0.52 respectively. There was statistical significant difference for Creatinine values of Group IV, between 7th, 14th and 28th day. The details are shown in the Table 13.

4.5.2 The Mean ± SE Values of Blood Urea Nitrogen (mg/dl) (on zero & 28th day):

The mean ± SE values of Blood Urea Nitrogen of Group I , Group II, Group III and Group IV on zero day were67.3 ± 9.73, 94.12 ± 19.02, 68.05 ± 11.13 and 78.15 ± 13.57 respectively.

The mean ± SE values of Blood Urea Nitrogen of Group I, Group II, Group III and Group IV on 28^{th} day were 107.17 ± 11.69, 50.83 ± 15.45, 31.14 ± 3.23 and 33.34 ± 7.66 respectively. There was no statistical significant difference between Groups at $P<0.01$. The details are shown in the Table 14.

4.6 Survival Rate of Animals in Different Groups at Different Intervals:

Of the ten animals in Group I which received the **conventional treatment**, two animals survived where as eight animals died. Out of the ten animals in Group II which received the specific therapy of **Punarnawadi Mandur** with conventional treatment, six animals survived where as four animals died during the treatment period. Out of the ten animals in Group III which received the specific therapy of **Azodyl** with conventional treatment nine animals survived where as one animal died during the treatment period. Out of the ten animals in Group IV, which received the specific therapy of **Rubenal** with conventional treatment, seven animals survived where as three animals died. The details are shown in the Table 15.

Table 1: Breed-Wise Occurrence of Renal Failure in Dogs (*n* =40)

Breed	Total	Percentage
Labrador Retriever	15	37.5
Non-descript	11	27.5
German Shepherd	7	17.5
Pomeranian (Spitz)	2	5
Cocker Spaniel	2	5
Dobermann Pinscher	1	2.5
Lhasa Apso	1	2.5
Great Dane	1	2.5
Total	**40**	**100**

Table 2: Gender-Wise Occurrence of Renal Failure in Dogs (*n*=40)

Gender	No. of dogs	Percentage
Male	26	65
Female	14	35
Total	**40**	**100**

Fig. 1: Breed-wise Occurrence of Renal Failure in Dogs

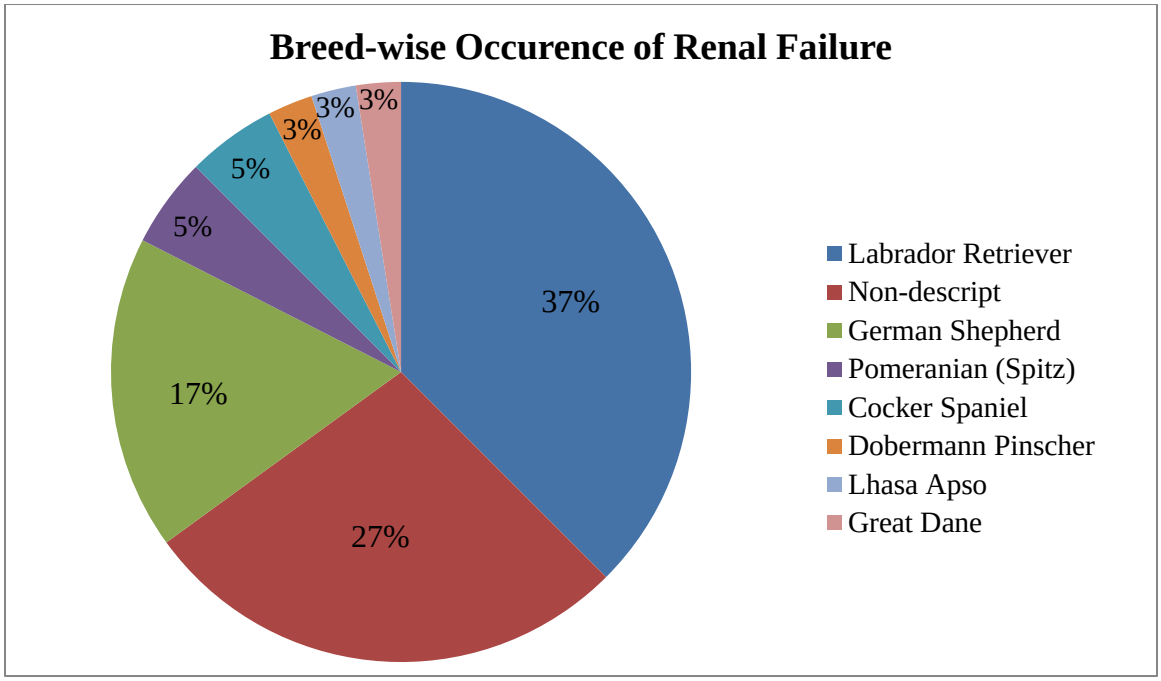

Fig. 2: Gender-wise Occurrence of Renal Failure in Dogs (*n* =40)

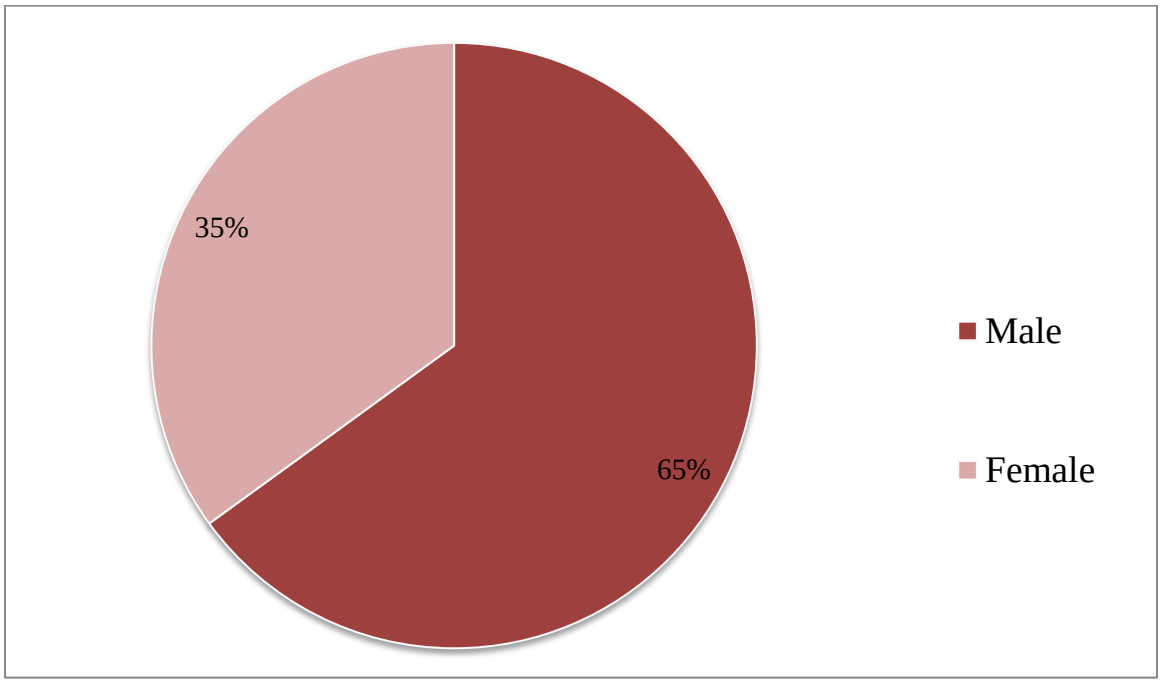

Table 3: Age-wise Occurrence of Renal Failure in Dogs (*n*=40).

Age	No. of Dogs affected	Percentage
up to 1yr	0	0
>1 to 5	5	12.5
>5 to 10	24	60
>10 to 15	11	27.5
Total	**40**	**100**

Fig. 3: Age-wise Occurrence of Renal Failure in Dogs (*n*=40).

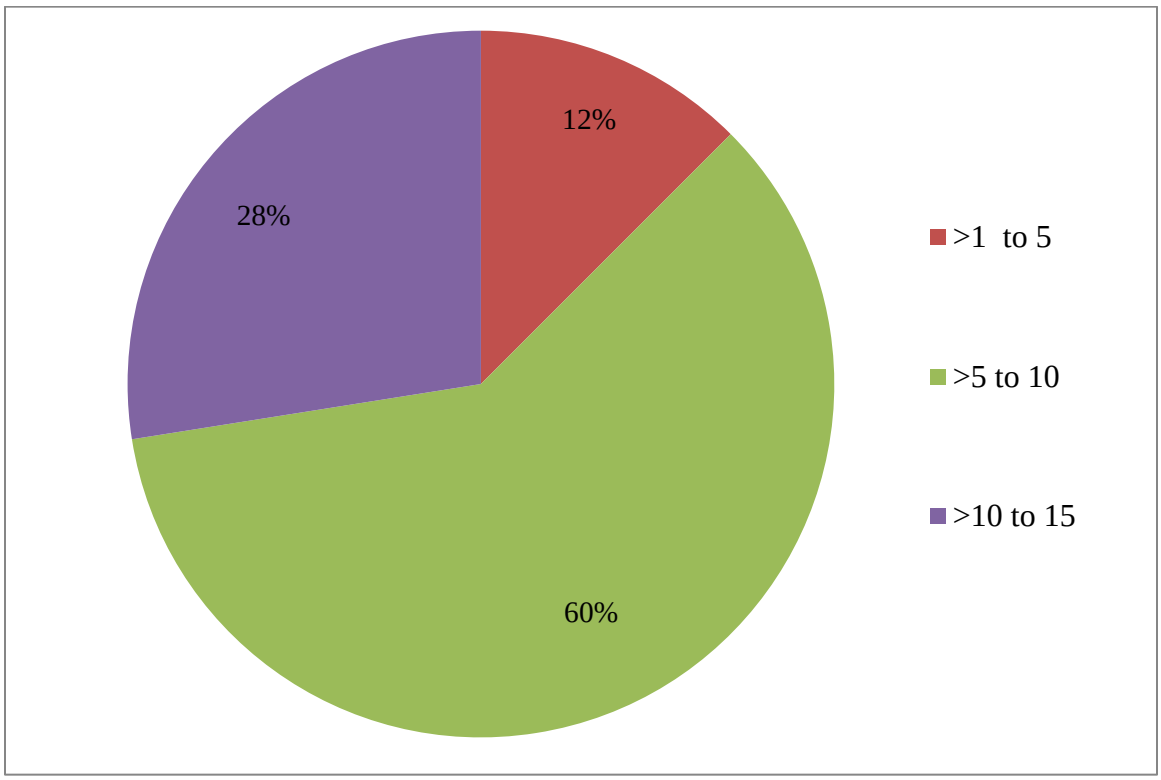

Table 4: Clinical Manifestations Exhibited by Dogs with Renal Failure (*n* =40).

Symptoms	No. of dogs	Percentage
Weakness	33	82.5
Anorexia	30	75
Weight loss	28	70
Pale mucous membrane	26	65
Vomition	25	62.5
Polyuria/Polydipsia	24	60
Poor hair coat	22	55
Emaciated body condition	15	37.5
Nervous signs	11	27.5
Diarrhoea	8	20
Halitosis	7	17.5
Oral ulcers	7	17.5
Congested mucous membrane	3	7.5

Table 5: Duration of Illness of Renal Failure Dogs before Presenting to the Hospital

Duration	No of animals	Percentage
0 – 5 days	8	20
6 – 10 days	9	22.5
>10 days	23	57.5
Total	**40**	**100**

Table 6: Food Habits of the Renal Failure Dogs

Type of food	No of animals	Percentage
Vegetarian	9	22.5
Veg + Egg	12	30
Non - vegetarian	19	47.5
Total	**40**	**100**

Table 7: Urine Specific Gravity (USG) Findings in Renal Failure Dogs.

Range	No of animals	Percentage
1.007-1.015	13	32.5
1.016-1.030	23	57.5
1.030 & above	4	10
Total	40	100

Fig. 4: Urine Specific Gravity (USG) Findings in Renal Failure Dogs.

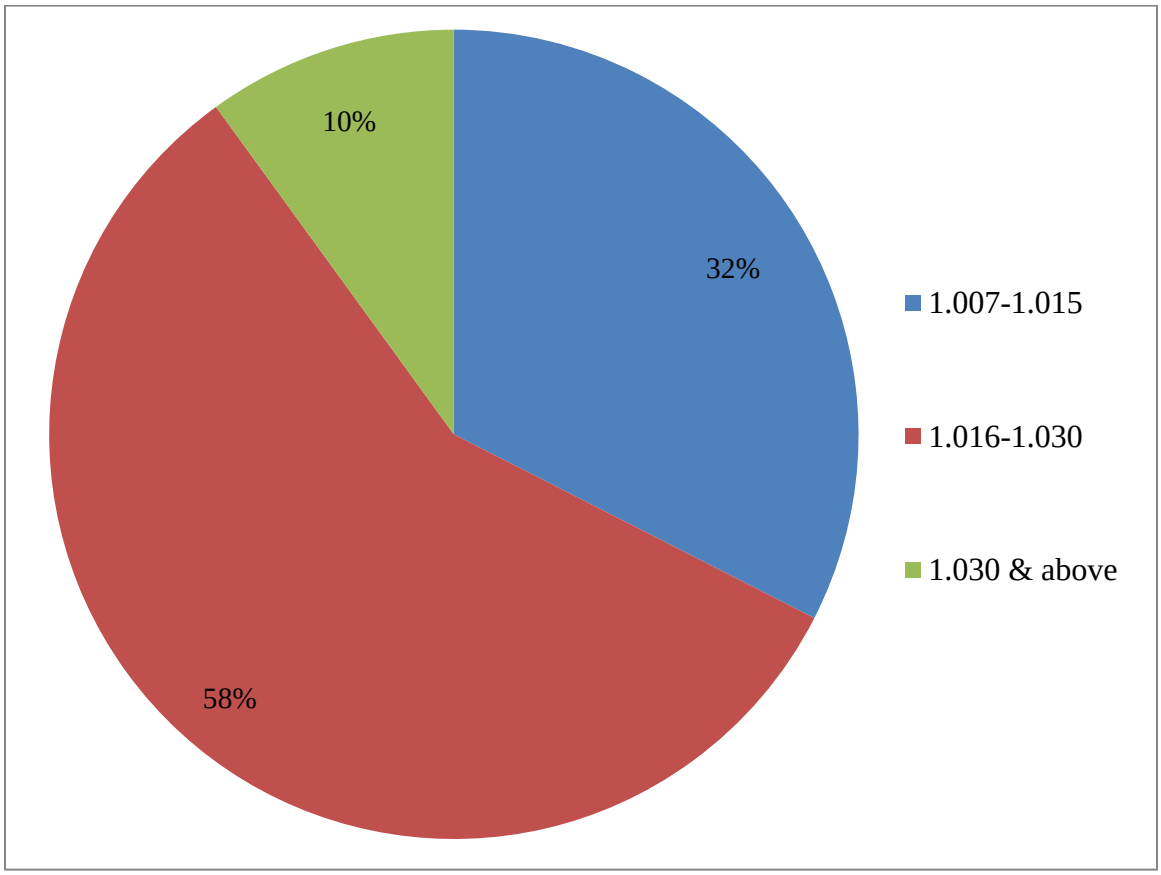

Table 8: Ultrasonographic Findings in Renal Failure Dogs

Findings	No of dogs	Percentage
End stage kidney (Small kidneys with loss of corticomedullary demarcation)	20	50
Nephritis (Increased cortical echogenicity)	3	7.5
Nephrocalicinosis (Multiple hyperechoic structures in the renal parenchyma)	2	5
Renal Cyst (Small spherical intercortical anechoic structures)	1	2.5
Normal Clear corticomedullary demarcation)	14	35
Total	**40**	**100**

Fig. 5: Ultrasonographic Findings in Renal Failure Dogs

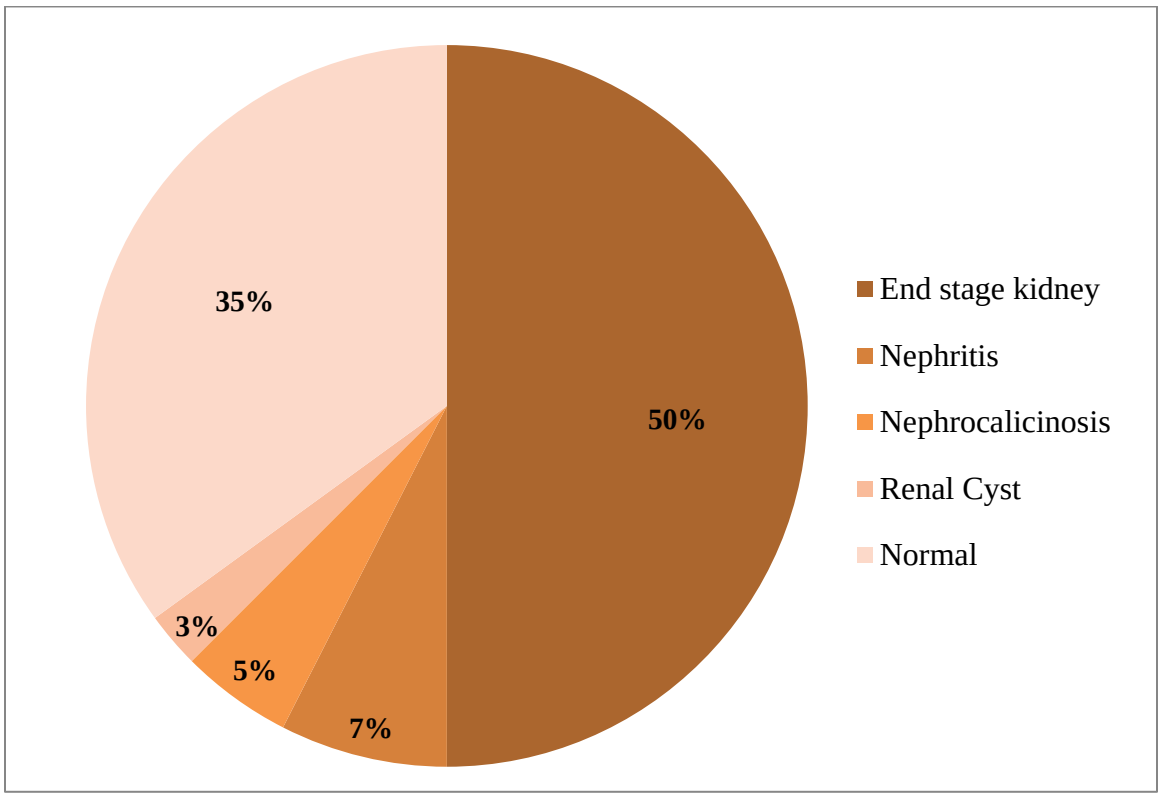

Table 9: Haematology and Biochemistry of Renal Failure Dogs (Zero day)

	Haematology					Biochemistry	
	TLC/ul	**PCV %**	**Hb gm/dl**	**PLT/ul**		**CRT mg/dl**	**BUN mg/dl**
1	13400	28.6	9.10	704000		6.50	98.2
2	18400	27.0	8.70	198000		6.70	91.0
3	8000	22.2	7.70	296000		5.00	40.0
4	14800	28.6	8.00	169000		5.70	67.0
5	11700	37.5	10.8	155000		10.1	73.2
6	3000	21.0	6.70	77000		10.4	123.0
7	10400	34.4	13.1	220000		19.0	223
8	11100	41.0	12.8	611000		4.50	67.0
9	10700	42.8	13.8	246000		3.40	29.0
10	8200.0	25.9	8.30	355000		8.90	182
11	17600	43.4	12.2	500000		3.90	57.0
12	18200	34.2	10.0	420000		2.20	25.0
13	14200	32.0	8.90	305000		16.0	96.0
14	10000	41.9	11.7	33000		5.40	48.0
15	6500	30.0	10.4	187000		9.80	120
16	7100	22.0	6.70	238000		17.0	137
17	6200	37.0	12.0	211000		6.10	78.0
18	10800	30.9	9.80	64000		2.30	63.0
19	4500	30.0	11.9	340000		3.10	67.0
20	13400	26.0	8.90	151000		3.90	47.0
21	15800	44.2	14.7	333000		4.30	49.0
23	14900	46.5	14.3	273000		2.90	36.0
24	11500	30.2	9.9	266000		8.60	120
25	12600	38.0	12.2	185000		3.90	62.3
26	13100	37.8	11.1	294000		4.10	49.5
27	13000	37.8	11.1	294000		4.10	49.5
28	8550	52.0	16.4	240000		7.40	97.0
29	12900	28.0	8.10	272000		5.90	46.8
30	8400	40.2	9.80	175000		6.50	112
31	15400	27.4	9.40	166000		2.40	57.0
32	7100	29.8	12	273000		24.0	235
33	6500	47.3	15.3	154000		2.70	34.0
34	18700	40.5	11.2	303000		15.3	166
35	8200	19.3	5.90	221000		6.9.0	146
36	15000	61.5	16.2	134000		2.72	70.3
37	6600	43.9	12.9	221000		2.10	43.0
38	7200	29.9	8.50	215000		2.80	56.4
39	12200	46.4	7.60	158000		9.80	132
40	8500	19.0	5.80	379000		3.20	39.2
Mean ± SE	10998.75 ± 642.7018	34.7625 ± 1.492428	10.66 ± 0.43	258600 ± 20906.1		6.15 ± 0.670	76.90 ± 6.86

Table 10: Classification of Renal Failure Dogs According to International Renal Interest Society Standards Based on Serum Creatinine Levels

Stage of renal failure	No of dogs	Percentage
Stage I	0	0
Stage II	0	0
Stage III	20	50
Stage IV	20	50
Total	**40**	**100**

Fig. 6: Classification of Renal Failure Dogs According to International Renal Interest Society Standards Based on Serum Creatinine Levels

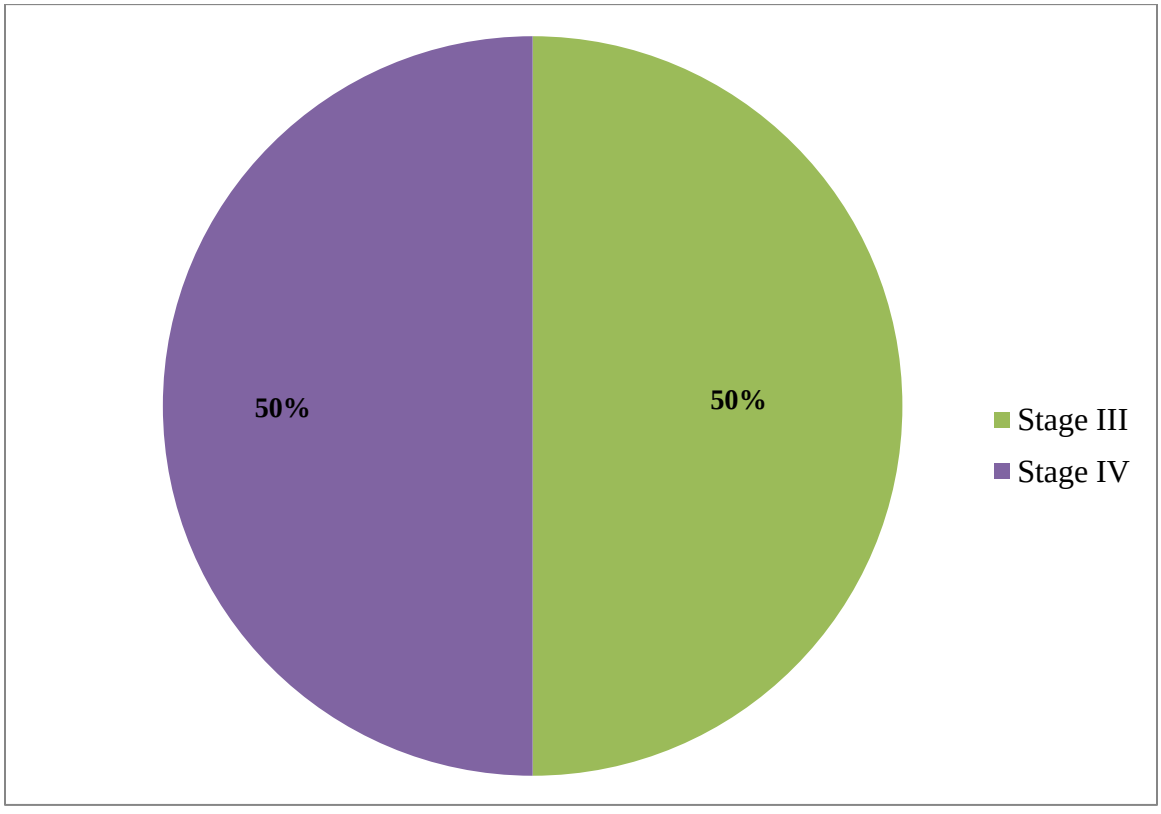

Table 11: Mean ± SE Values of Hemoglobin (gm/dl) in Renal Failure Dogs

Day / Group	Zero	3rd	7th	14th	28th
Group I	9.57 ± 0.42	9.13 ± 0.44	8.12 ± 0.58	7.3 ± 0.58	7.27 ± 1.05
Group II	11.36 ± 0.92	10.66 ± 0.76	10.52 ± 0.75	11.06 ± 0.78	10.62 ± 0.81
Group III	12.03 ± 0.95	11.55 ± 1.07	10.52 ± 0.87	10.83 ± 1.01	12.16 ± 0.69
Group IV	9.7 ± 0.93	9.75 ± 0.84	9.17 ± 0.94	9.21 ± 1.14	11.11 ± 1.03

Fig.7: Mean ± SE Values of Hemoglobin (gm/dl) in Renal Failure Dogs

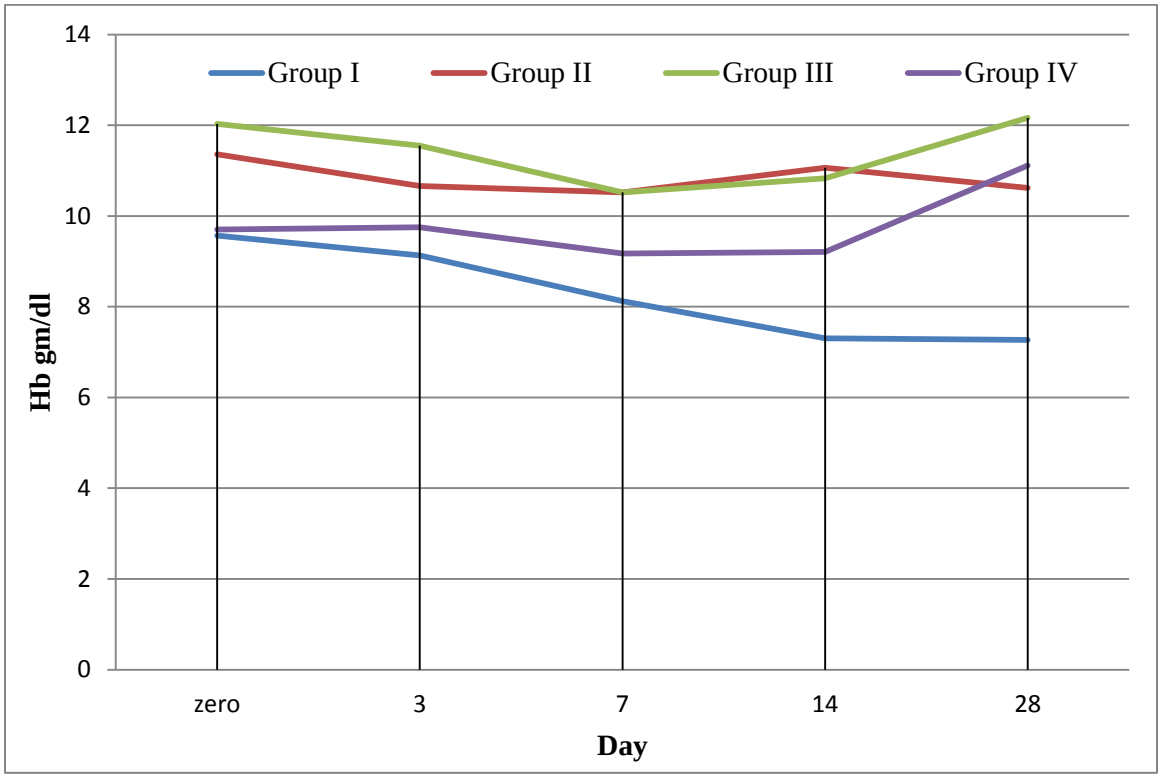

Table 12: Mean ± SE Values of PCV (%) in Renal Failure Dogs

Day / Group	Zero	3rd	7th	14th	28th
Group I	29.69 ± 1.34	28.05 ± 1.08	25.63 ± 1.99	24.14 ± 1.68	23.1 ± 3.94
Group II	38.1 ± 3.39	35.48 ± 2.34	35.61 ± 2.35	36.6 ± 1.76	34.02 ± 2.04
Group III	37.06 ± 3.21	34.71 ± 3.24	32.63 ± 2.78	34 ± 2.97	37.94 ± 2.46
Group IV	34.2 ± 3.21	34.94 ± 2.99	32.59 ± 3.03	33.64 ± 3.41	38.96 ± 0.95

Fig. 8: Mean ± SE Values of PCV (%) in Renal Failure Dogs

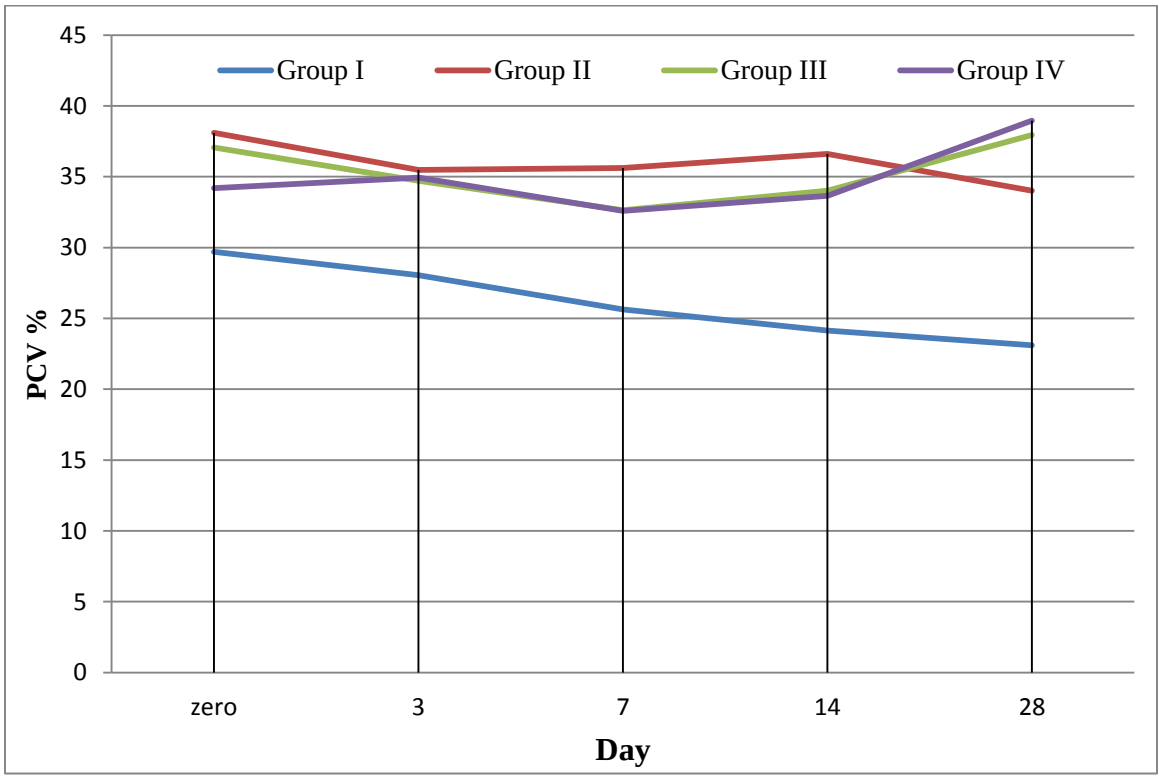

Table 13: Mean ± SE Values of Creatinine (mg/dl) in Renal Failure Dogs

Day / Group	Zero	3rd	7th	14th	28th
Group I	6.3 ± 1.27	6.65 ± 1.4 (-5.5)	9.42 ± 2.29 (-49.5)	6.64 ± 1.11 (-5.39)	5.87 ± 0.18 **(6.83)**
Group II	7.63 ± 1.89	8.71 ± 2.37 (-14.15)	9.27 ± 2.67 (21.49)	4.4 ± 1.01 (57.6)	3.4 ± 0.74 **(44.56)**
Group III	5.26 ± 0.86	5.4 ± 1.33 (-2.66)	5.12 ± 1.58 (2.67)	3.19 ± 0.46 (39.35)	2.76 ± 0.32 **(47.5)**
Group IV	5.01 ± 0.9[a]	4.24 ± 0.95[b] (15.37)	3.76 ± 0.82[b] (24.9)	4.03 ± 1.12[b] (19.56)	2.13 ± 0.52[b] **(57.5)**

Values in parenthesis indicate the percent improvement of the Creatinine in terms of reduction in values compared to the zero day value.

Significant at P≤0.05

Common superscript Row= ab

Means bearing any one of the common superscript in a row do not differ significantly with each other.

Fig. 9: Mean ± SE Values of CRT (mg/dl) in Renal Failure Dogs

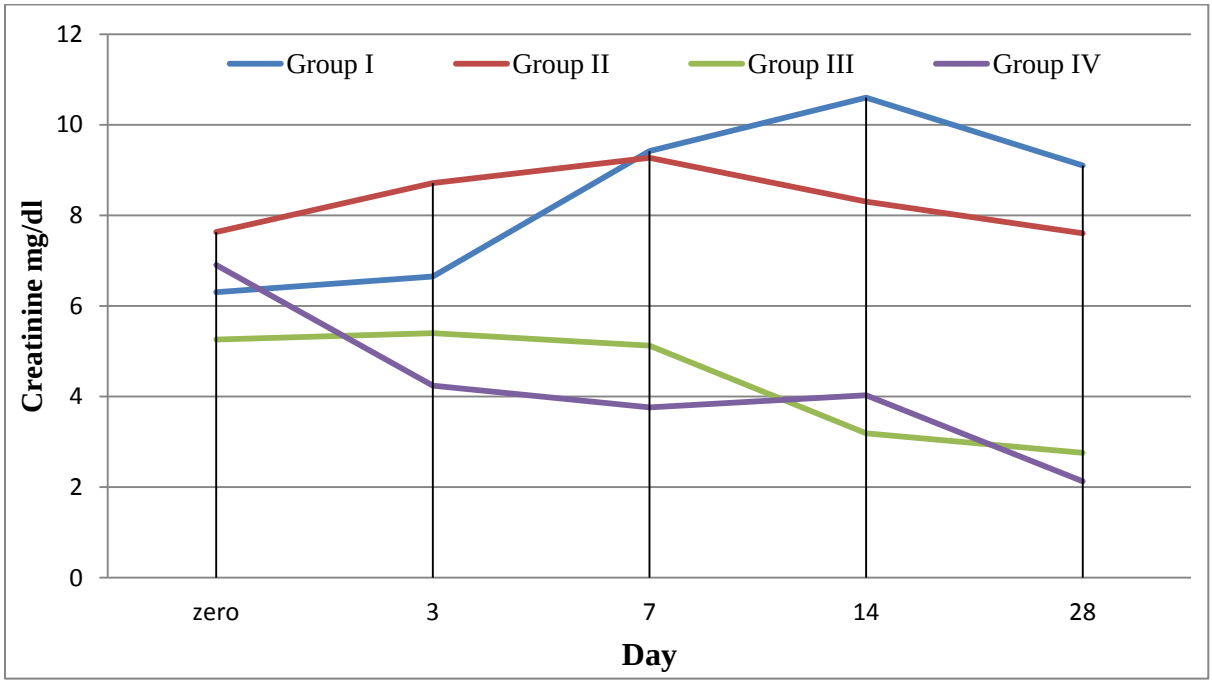

Table 14: Mean ± SE Values of BUN (mg/dl) in Renal Failure Dogs

Day / Group	Zero	3rd	7th	14th	28th
Group I	67.3 ± 9.73	80.6 ± 10.66	119.1 ± 20.89	97 ± 11.79	107.17 ± 11.69 **(-59)**
Group II	94.12 ± 19.02	94.52 ± 20.59	103.19 ± 23.65	62.5 ± 12.99	50.83 ± 15.45 **(46)**
Group III	68.05 ± 11.13	65.76 ± 14.36	59.4 ± 18.9	36.42 ± 5.83	31.14 ± 3.23 **(54.25)**
Group IV	78.15 ± 13.57	72.82 ± 14.46	49.3 ± 8.16	56.2 ± 15.35	33.34 ± 7.66 **(57.4)**

Fig. 10: Mean ± SE Values of BUN (mg/dl) in Renal Failure Dogs

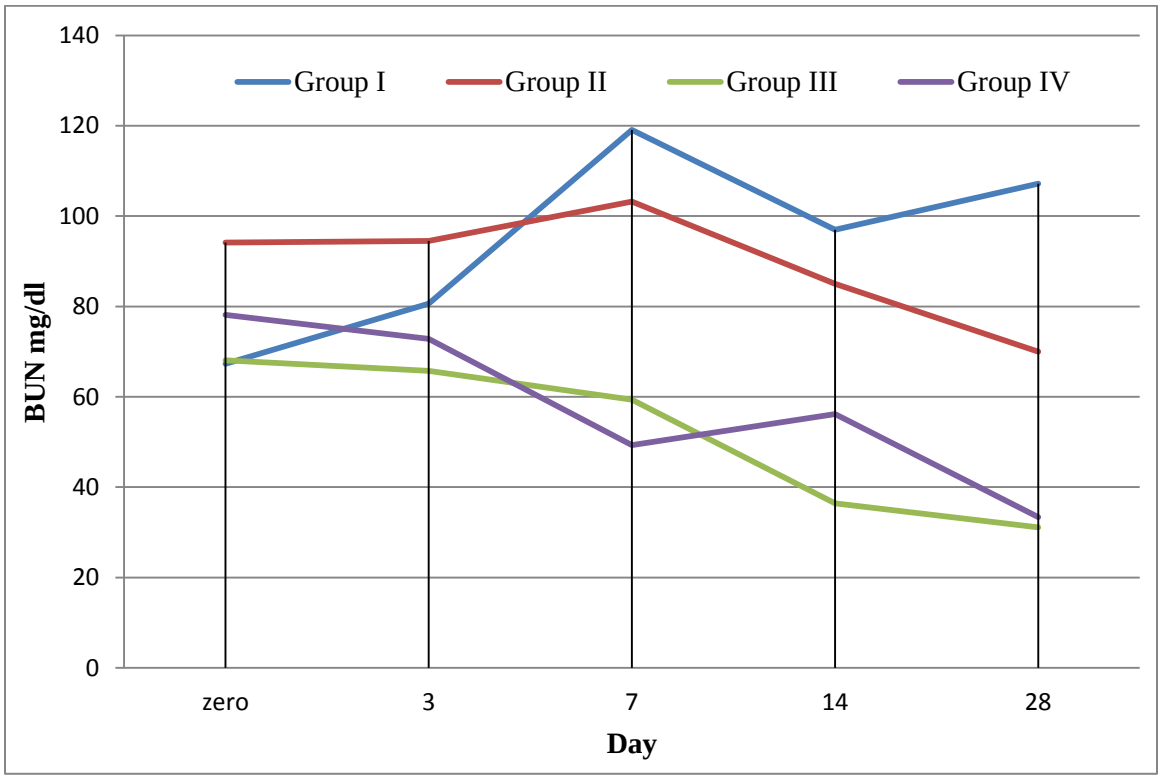

Table 15: Survival Rate of Animals in Different Groups at Different Intervals

Day / Group	Zero	3rd	7th	14th	28th
Group I	10/10	10/10	5/10	3/10	2/10 **20%**
Group II	10/10	10/10	7/10	7/10	6/10 **60%**
Group III	10/10	10/10	10/10	10/10	9/10 **90%**
Group IV	10/10	10/10	10/10	10/10	7/10 **70%**

Discussion

V. DISCUSSION

5.1 Diagnosis of renal of renal failure

5.1.1 Clinical manifestation

History collection is very important to make diagnosis, and this should be correlated with the physical examination.

The clinical signs observed in renal failure cases in the present study have been presented in the Table 4.The predominant signs noticed were weakness 33 (82.5%), anorexia 30 (75%), weight loss 28 (70%), pale mucous membrane (65%), vomition 25 (62.5%), PU/PD 24 (60%), poor hair coat 22 (55%), nervous sign 11 (27.5%), diarrhoea 8 (20%), halitosis 7 (17.5) and oral ulcers 7 (17.5%). The findings are similar to the findings of earlier workers Rubin, (1997) and Meyer, (2004).

In the present study, weakness was the most common clinical sign and was noticed in 82.5 per cent cases. Weakness in renal failure occurs due to variety of causes. It may be consequence of dehydration, prolonged anorexia or hypokalemia as indicated by Kralova *et al.*, (2009).

In the present study anorexia was recorded in 75 per cent of the renal failure dogs. It is one of the common clinical manifestations in the renal failure dogs. Anorexia may be due to dehydration, anaemia and increased levels of uremic toxins due to renal failure. However Osborne *et al.,* (1995) stated that nausea and altered taste sensation due to increased levels of urea, ammonia and other retained toxins in saliva may also contribute to anorexia.

Vomition was recorded in 62.5 per cent of the renal failure cases in present study. Vomition is one of the common clinical sign in renal failure. Vomiting is a frequent, but inconsistent finding resulting from the effects of uremic toxins on the medullary emetic chemoreceptor trigger zone and uremic gastroenteritis. Renal failure results in decreased clearance of gastrin and increased gastric acid production which exacerbates the gastric lesions as indicated by Osborne *et al.,* (1995); Thornhill, (2000) and Polzin, (2011) and this is also one of the contributing factors for renal failure.

In the present study polydipsia and polyuria was observed in sixty per cent of the renal failure dogs. These findings are similar to observations made by earlier workers Robinson *et al*., (1989). The high frequency of polyuria and polydipsia may be due to inability of kidneys to concentrate urine as opined by Vaden *et al.,* (1998).

Nervous signs like change in the behaviour and lethargy were observed in 27.5 per cent of the renal failure dogs in the present study. Nervous signs in the renal failure dogs may be due to the accumulation of nitrogenous substances in the blood, dehydration and electrolyte disturbances and this can lead to the uremic encephalopathy if the cases are complicated by uremia, thiamine deficiency and hypertension as indicated by Scaini *et al.,* (2010).

Oral ulcers were observed in 17.5 per cent of renal failure dogs in the present study. The oral lesions may be due to the caustic effects of ammonia produced locally by the action of bacterial ureases, as evidenced by the fact that BUN levels were higher (>25 mg/dl) in the renal failure dogs in the present study. Similar observations have been reported earlier by Robinson *et al.,* (1989) and Forrester and Brandt (1994).

5.1.2 Urine Specific Gravity (USG):

Urine specific gravity observed in the present study was in the range of 1.008 to 1.035 with the mean of 1.019 ± 0.0012. In the present study 13 dogs were having urine specific gravity in the range of 1.007 to 1.015, which indicates isosthenuria. Isosthenuria develops when 67 per cent of nephrons become non-functional. Twenty three dogs were having urine specific gravity in the range of 1.016 to 1.030, and this indicates submaximally concentrated urine (USG <1.029) and loss of urine concentrating ability in renal failure. So urine specific gravity can be used as one of the markers for early diagnosis of renal failure in dogs. These finding are similar with the observations of McGrotty (2008) who stated that the azotemic patients with early renal dysfunction may have inadequate concentrating ability. The remaining four animals had normal urine specific gravity (>1.030).

5.1.3 Ultrasonographic study in renal failure dogs:

In the present study out of 40 cases, twenty eight cases showed the ultrasonographic changes in the kidneys. It is observed from Table 8 that twenty cases were end stage kidneys (50%), three cases nephritis (7.5%), two cases nephrocalcinosis (5%) and one showed renal cyst (2.5%). Earlier workers Gonenci *et al.,* (2003); Pallavi *et al.,* (2006); Vijaykumar *et al.,* (2011) has indicated that ultrasonography can be used for diagnosis of renal disease. In the present study, 65 per cent cases showed changes in the kidneys based on the ultrasonography. Based on these observations in the current study, it can be construed that ultrasonography can be used as a quick and convenient method for early diagnosis of renal failure.

5.1.4 Hematology :

In the present study, the haematological parameters TLC, PCV, Hb and platelet of renal failure dogs have been depicted in Table 6, 7, 8 and 9 respectively.

The TLC values observed in this study are depicted in Table 9. Mean ± SE values of Total Leukocyte Count/ul of Group I, Group II, Group III and Group IV on zero day were10950 ± 1187.64, 12760 ± 1253.37, 8965 ± 1228.37 and 11320 ± 1361.44 respectively. In the present study total leukocyte count was enumerated to rule out the cases of infectious origin and results indicate that cases selected were having normal TLC values.

In the present study hemoglobin and hematocrit values are depicted in the Table 11 and 12. The mean ± SE values of Hb (gm/dl) of Group I , Group II, Group III and Group IV on zero day were 9.7 ± 0.93, 10.95 ± 0.86, 12.23 ± 0.952 and 9.36 ± 0.37 respectively. And the mean ± SE values of PCV% of Group I , Group II, Group III and Group IV on zero day were 34.2 ± 3.21, 38.44 ± 3.37, 36.72 ± 3.22 and 29.69 ± 1.34 respectively. In the present study, 70 per cent of the dogs were having haemoglobin values less than normal (5.6 to 11.9 g %). The normal haemoglobin value in dogs is 12 to 17 gm/dl. It indicates the anemia due to renal failure. These findings are similar with the findings of Robinson *et al*., (1989). According to Polzin (2011) as renal function declines in patients with renal disease, a normocytic normochromic hypoproliferative anemia typically develops and the severity of anemia is roughly proportional to the loss of kidney function. Anaemia in renal failure could be due to reduced renal production of erythropoietin, reduced red blood cell survival, gastrointestinal bleeding, uremic

inhibitors of erythropoiesis, marrow fibrosis, and nutritional deficiencies as indicated by Cowgill (1992).

5.1.5 Creatinine and Blood Urea Nitrogen:

In the present study serum creatinine values were used to establish the diagnosis of suspected renal failure cases. Those animals which were having serum creatinine value more than 1.4 mg/dl were diagnosed as renal failure and included in the study.

The mean ± SE values of creatinine (mg/dl) of Group I , Group II, Group III and Group IV on zero day were 5.01 ± 0.9, 6.55 ± 1.63, 6.75 ± 1.604 and 9 ± 2.07 respectively. The values of serum creatinine in these 40 cases, ranged between 2.1mg/dl to 19 mg/dl with a mean of 6.1mg/dl. These values indicate renal damage. The normal serum creatinine value for dogs is <1.4 mg/dl. In the present study the serum creatinine has been considered the main biological marker to evaluate the renal failure cases. International Renal Interest Society for canines has proposed staging system based on the serum creatinine values. In the present study, 50 per cent cases were found in the stage three (Crt 2.1-5 mg/dl) and 50 per cent cases were found in the stage four (Crt >5 mg/dl) renal failure. Earlier workers Gleadhill, (1994); Braun and Lefebvre, (2005) stated that an abnormally high serum creatinine value is assumed to indicate the loss of at least 65-75 per cent of functional renal mass. So serum creatinine can be used as good biochemical marker of the renal failure. Serum creatinine concentration increases as a result of the progression of renal disease and decline of glomerular filtration rate (Finco and Duncan, (1976), and DiBartola, (2000).

Increase in urea levels in renal failure is one of the common features and caused by impaired ability to excrete proteinaceous catabolites because of marked reduction in glomerular filtration rate (GFR). In the present study, the mean ± SE value of Blood Urea Nitrogen (mg/dl) of Group I, Group II, Group III and Group IV on zero day was 85.35 ± 16.94, 76.77 ± 12.89, 85.4 ± 18.8 and 89.12 ± 18.53 respectively. The BUN values in these 40 cases ranged between 25 to 223 mg/dl with the mean of 76.90 mg/dl. According to International Renal Interest Society (IRiS) for canines, the BUN values 80 mg/dl and above is a sign of uremia due to impaired kidney function. The values less than 80 mg/dl is more reflective of other factors such as dehydration, stress, high protein diet, gastrointestinal haemorrhages and less reflective of stage of kidney disease as compared to the creatinine value. In the present study it is observed from Table 9 that 19 dogs were in uremic stage (47.5%). So from above observations it can be stated that the BUN is not kidney specific and is a poor marker for early diagnosis of renal falure. These findings are similar with the observations of Kralova *et al.,* (2009); Pradhan and Roy (2012); Kavitha *et al*., (2013).

5.2 Occurrence of renal failure:

In the present study 40 cases were confirmed as renal failure cases based on history, physical examination, haematology, biochemistry, urine specific gravity and ultrasonography. In the present study, the level of serum creatinine was used as an indicator for diagnosis of renal failure. Based on this, occurrence of renal failure has been presented.

5.2.1 Breed-wise occurrence of renal failure:

In the present study, it is observed from the Table 1 that the occurrence of renal failure in different breeds of dogs ranged from 2.5 per cent to 37.5 per cent. The occurrence was highest in the Labrador Retriever (37.5%) and Non-descript (27.5%) followed by GSD (17.5%), Pomeranian (5%), Cocker Spaniel (5%), Great Dane (2.5%), Doberman (2.5%), Lhasa Apso (2.5%). These findings are similar with the findings of Kandula & Satishkumar, (2014) who reported that incidence of renal failure highest in Labrador retriever and GSD and lowest in Pomeranian and mixed breeds. The present findings related to breed-wise prevalence are in accordance with Saravanan *et al*. (2012) who documented high prevalence of renal failure among Labrador breed. The occurrence of renal failure is more common in some breeds than in others and this can probably be attributed to the popularity of certain breeds in this geographical location.

5.2.2 Gender-wise occurrence of renal failure:

Out of 40 cases of renal failure based on serum creatinine values in the present study, it can be observed from Table 2 that 65 per cent were males and 35 per cent were females and male dogs suffered more frequently than female dogs. This agrees with the findings of Behrend *et al.,* (1996) who reported that the incidence of renal failure was slightly greater in the males as compared to the females. This may probably be due to the higher number of males presented to the clinics as compared to females. Further in the present study, 65 percent of dogs screened were males which might account for higher occurrence. But above findings are in contrast with the observations made by Kandula & Satishkumar, (2014) who reported highest occurrence of renal insufficiency in female

dogs as compared to males. The highest incidence of most of renal disorders in female dogs might be due to various unhygienic managemental practices during peurperal stage that may lead to genital infection, which may progress as urogential complaints as stated by Tilley and Smith, (2007).

5.2.3 Age-wise occurrence of renal disease:

In the present study, the highest incidence of renal disease was found in 5 to 10 years age of group of dogs (60%), followed by 10 to 15 years (27%) and 1 to 5 years (12.5%). The average age of occurrence of renal failure was 8.5 years. These findings are in agreement with Kralova *et al*., (2010) and Kavitha *et al*., (2013) who opined that renal disorders were common complaints among aged dogs that were above 8 years of age and risk increases with age. This might be due to the fact that with advancing age blood flow to the kidney decreases and there is a loss of nephrons, the resorption process with in the prevailing nephrons also gets impaired with advance in age (Grauer and Lane, 1995).

5.3 Therapeutic trials:

In the present study, 40 cases diagnosed as renal failure cases mainly based on the serum creatinine values were used for therapeutic study.

It can be observed from the Table 11 and 12 that in Group I, the haemoglobin value on zero day was 9.27±0.42 and on 28^{th} day it was 7.27±1.05. There was no statistical significant difference between the values in this group. Further there was no apparent improvement in the Hb and PCV values and there was progressive decline in the haemoglobin values which indicates persistence of anemia in renal failure.

The creatinine values in the Group I cases on zero day, 3rd day, 7th day, 14th day and 28th day were 6.3 ± 1.27, 6.65 ± 1.4, 9.42 ± 2.29, 6.64 ± 1.11 and 5.87 ± 0.18 respectively. There was increase in the creatinine values on 7th day and further 8 dogs died between 7th day and 28th day and two dogs survived during the treatment period. Survival rate in Group I was 20%. Overall there was no decrease in creatinine values in this group. Within one week the values of creatinine increased from the 6.3 to 9.4 mg/dl, which indicates that there was progressive deterioration of kidney function and the effect of the treatment was not apparent to restore the normal renal function. Further in the present study, it can be observed from the Table 14 that the BUN values were progressively increasing during the treatment period. The mean of BUN values on zero day was 67.3 mg/dl and it increased to 107.17 mg/dl at the end of treatment period. So from above findings it can be concluded that the renal function was progressively deteriorating in the conventional treatment group and the conventional treatment could not help in the improvement of kidney function and health of the animals during treatment period. These findings are similar with the findings of earlier workers Brown, (1999) and Roudebush *et al.,* (2010) who stated that conservative management of renal failure should not be expected to halt, reverse or eliminate renal lesions responsible for kidney disease and therefore management strategies are most beneficial when combined with specific therapy.

The Group II animals which received the specific therapy with Punarnava (Punarnawadi Mandur) along with conventional treatment did not show any improvement in the haemoglobin and PCV values during the treatment period. These values progressively reduced during therapeutic period. Thus Punarnava did not help in the

improvement of anemia in the present study. These findings are in contrast with the observations made by Bhowmik *et al* (2012) who reported that Punarnava is beneficial in the treatment of anemia. Further it is observed from Table 13 and 14 that creatinine and BUN values were progressively decreasing at the end of treatment period. There was 44.56 per cent of improvement in the creatinine value on 28th day from the initiation of treatment. This indicates that there was progressive improvement in the renal function during the treatment period. These findings are similar with the observations made by Pareta *et al.,* (2011) and Pradhan and Roy (2012). In Group II, six animals survived during the treatment period (survival rate 60%). Overall findings in Group II shows that there was improvement in the renal function.

In the present study, Group III received specific therapy of probiotics (Azodyl) with conventional treatment. In this group there was no apparent improvement in the Hb and PCV values during the treatment period which indicates there is no effect of probiotics to improve the haematological parameters in renal failure dogs. Results showed progressive decline in the BUN and creatinine over time. There was 47.5 per cent decrease in the serum creatinine level in this group. These findings are similar with the observations of earlier workers Palmquist, (2006); Rangnathan *et al.,* (2009); McCain *et al.,* (2011). Survival rate in Group III was 90 per cent, only one animal died between 14th and 28th day. Overall findings showed that probiotics are helpful in the improvement of renal function. The mechanism how probiotics reduces the creatinine level in renal failure is unknown but probiotic bacteria having affinity towards the uremic toxins which is absorbed from the intestines. So this might be the reason to improve the overall status of renal failure cases after treatment with probiotics (Azodyl).

In Group IV dogs which received the specific therapy of Rhubarb (Rubenal) along with conventional treatment, it can be observed from Table 11 and 12 that there was apparent improvement in the Hb and PCV values during the treatment period. This shows that Rubenal helped in improvement in the haematological parameters in renal failure dogs. These findings are in agreement with Khan *et al* (2014) who reported similar findings in their study on randomized clinical trial in humans for evaluation of Rhubarb supplementation in Stage 3 and 4 of chronic kidney disease. Creatinine and BUN values decreased from zero day to 28^{th} day after the start of treatment with Rubenal. There was statistical significant difference ($P<0.05$) between creatinine values in Group IV on 7^{th} day, 14^{th} day and 28^{th} day. The per cent improvement in the creatinine value was 57.5. When compared to the conventional treatment group, improvement in terms of reduction in the creatinine value was very high. This shows that there was significant improvement in the creatinine level on 7^{th} day, 14^{th} day and 28^{th}. During the study in Group IV, 7 animals survived (survival rate 70%) and three animals died between 14^{th} and 28^{th} day. Rubenal contains various phytoconstituents among which rhein and emodin are important because of their beneficial effect in CKD. Rhein inhibits cell hypertrophy and extracellular matrix (ECM) accumulation by decreasing the transforming growth factor-beta 1 (TGF-β1) and fibronectin expression in renal tissue. Emodin inhibits mesangial cell proliferation. Rhubarb also has laxative effect which increases excretion of nitrogenous wastes from the body as described by Hu *et al.,* (1991); Liu *et al.,* (1992); Gao *et al.,* (2010). These might be the probable mechanisms for beneficial effects of Rubenal in the current study.

5.4 Comparison between therapeutic regimens

In the present study, results showed that the survival rate in Group I, II, III and IV was 2/10 (20%), 6/10 (60%), 9/10(90%) and 7/10 (70%) respectively. As regards the Hb and PCV, there was no statistical difference between the values in any group on respective treatment dates. The per cent decrease in the creatinine values in Group I, II, III and IV were 6.83%, 44.56%, 47.5% and 57.5% respectively. The per cent decrease in BUN values for Group I, II, III and IV was -59%, 46%, 54% and 57.4% respectively. Based on all these observations it can be construed that the newer regimens in the current study, did not have effect on the Hb and PCV which indicates that the specific medications may not have positive effect on anemic status. These findings are similar with the observations of Sathiyapriya *et al.*, (2009); and Rengao *et al.*, (1995).

The Group IV animals which received Rhubarb supplementation (Rubenal) showed highest decrease (57.5%) in the creatinine values and highest decrease (57.4%) in BUN values, which indicated that Rubenal is superior to other compounds. These findings are similar with the Hu *et al.*, 1991; Liu *et al.*, (1992) and Khan *et al.*, (2014).

In the present study, based on the highest per cent survival (90%) in Group III animals which received Probiotic supplementation (Azodyl), superior to other treatment regimens, in terms of management of renal failure. These findings are similar with the observations made by Palmquist *et al.*, (2006) who noted the highest survival rate in the renal failure cats which received the therapy of probiotics.

Summary

VI. SUMMARY

Renal failure is one of the important problems in canines that cause considerable morbidity and mortality. The present study was conducted to evaluate the effect of different regimens of treatment to manage the renal failure cases. A total of 40 cases were diagnosed as renal failure based on history, clinical signs, hematology and biochemistry, urine specific gravity and ultrasonography and were included in the study.

These 40 renal failure cases were randomly allotted to four groups each group having 10 cases. Group I received conventional treatment, Group II received punarnava, Group III received Probiotic (Azodyl) and Group IV received rhubarb extract (Rubenal) therapy along with the conventional therapy.

In the present study these cases were evaluated based on the Hb, PCV, creatinine and BUN on zero, 3^{rd}, 7^{th}, 14^{th} and 28^{th} day after initiation of treatment.

The clinical signs encountered in renal failure cases were anorexia, weakness, vomition, dehydration, uremic breath, oral ulcers, anemia, poor hair coat, polyurea, polydypsia, and nervous signs, though some of these are not very specific to the renal problems.

In the present study breed-wise occurrence of renal failure was highest in Labrador Retriever (37.5%) and lowest in Doberman Pinscher (2.5%), Lhasa Apso (2.5%) and Great Dane (2.5%). Gender-wise occurrence was in more in males (65%) than in females (35%) and age-wise occurrence was highest in the 5-10 years age group (60%) and lowest in age group up to one year (0%).

The mean ± SE values of Hb (gm/dl) of Group I , Group II, Group III and Group IV on zero day were 9.57 ± 0.42, 11.36 ± 0.92, 12.03 ± 0.95 and 9.7 ± 0.93 respectively. The mean ± SE values of Hb of Group I , Group II, Group III and Group IV on 28^{th} day were7.27 ± 1.05, 10.62 ± 0.81, 12.16 ± 0.69 and 11.11 ± 1.03 respectively.

The mean ± SE values of PCV (%) of Group I , Group II, Group III and Group IV on zero day were 29.69 ± 1.34, 38.1 ± 3.39, 37.06 ± 3.21 and 34.2 ± 3.21 respectively. The mean ± SE values of PCV of Group I , Group II, Group III and Group IV on 28^{th} day were 23.1 ± 3.94,34.02 ± 2.04, 37.94 ± 2.46 and 38.96 ± 0.95 respectively.

The mean ± SE values of creatinine (mg/dl) of Group I , Group II, Group III and Group IV on zero day were 6.3 ± 1.27, 7.63 ± 1.89, 5.26 ± 0.86 and 5.01 ± 0.9 respectively. The mean ± SE values of creatinine of Group I , Group II, Group III and Group IV on 28^{th} day were 5.87 ± 0.18, 3.4 ± 0.74, 2.76 ± 0.32 and 2.13 ± 0.52 respectively. There was statistical significant difference ($P<0.05$) in Group IV on 7^{th} day, 14^{th} day and 28^{th} day.

The mean ± SE values of Blood Urea Nitrogen (mg/dl) of Group I , Group II, Group III and Group IV on zero day were 67.3 ± 9.73, 94.12 ± 19.02, 68.05 ± 11.13 and 78.15 ± 13.57 respectively. The mean ± SE values of Blood Urea Nitrogen of Group I, Group II, Group III and Group IV on zero day were 107.17 ± 11.69, 50.83 ± 15.45, 31.14 ± 3.23 and 33.34 ± 7.66 respectively. There was no statistical significant difference between the values between zero day and 28^{th} day ($P >0.05$).

In the present study Hb and PCV values did not improve in any of the group, which indicated that the treatment regimens followed did not improve the anemic status during study period.

Creatinine and BUN values were progressively decreasing in Group II, III and IV after start of treatment, however per cent reduction in the creatinine values in Group IV was highest (57.5%), followed by Group III (47.5%) and Group II (42%). Per cent reduction in BUN values was high in Group IV (57.4%) followed by Group III (54.25%) and Group II (46%).

In the present study in Group I which received conventional treatment, the mortality was 80 per cent (8/10) however the mortality in new regimen groups was 26.66 per cent (8/30). In the new regimen groups the highest survival rate found in the Group III followed by Group IV and Group II.

Based on the per cent decrease in creatinine value, Group IV animals which received Rhubarb supplementation (Rubenal) was superior to Group II and III. Further based on per cent survival, in Group II (60%), Group IV (70%) and Group III (90%), the Group III animals which received Probiotic therapy (Azodyl) was superior to other regimens.

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Abstract

VIII. ABSTRACT

The present study on therapeutic management of renal failure in dogs was carried out by subjecting the renal failure dogs to different regimens of treatment along with the conventional treatment. Renal failure in dogs diagnosed based on the clinical signs, hematology , biochemistry, urine specific gravity and ultrasonography. These 40 cases then randomly allotted to the four different groups each having ten dogs. Group I received conventional treatment, Group II received Punarnava along with conventional treatment, Group III received Probiotic therapy along with conventional treatment and Group IV received Rhubarb supplementation along with conventional treatment.

Per cent reduction in the creatinine values in Group IV was highest (57.5%), followed by Group III (47.5%) and Group II (42%). Per cent reduction in BUN values was high in Group IV (57.4%) followed by Group III (54.25%) and Group II (46%). Based on the per cent decrease in creatinine and BUN values, Group IV animals which received Rhubarb supplementation (Rubenal) was superior to Group II and III. In the present study in Group I which received conventional treatment, the mortality was 80% (8/10) however the mortality in new regimen groups was 26.66% (8/30). Further based on per cent survival, in Group II (60%), Group III (90%) and Group IV (70%), the Group III animals which received Probiotic therapy (Azodyl) was superior to other regimens.

Appendices

IX. APPENDICES

Appendix I: Urine Specific Gravity Values in Renal Failure Dogs

Sl. No	Specific Gravity	Sl. No	Specific Gravity
1	1.018	21	1.008
2	1.008	22	1.025
3	1.024	23	1.02
4	1.018	24	1.03
5	1.014	25	1.035
6	1.03	26	1.016
7	1.024	27	1.018
8	1.02	28	1.015
9	1.028	29	1.02
10	1.018	30	1.024
11	1.02	31	1.008
12	1.018	32	1.012
13	1.015	33	1.008
14	1.014	34	1.032
15	1.016	35	1.015
16	1.028	36	1.02
17	1.02	37	1.028
18	1.028	38	1.021
19	1.015	39	1.018
20	1.015	40	1.012

Appendix II: Hemoglobin (gm/dl) Values in Renal Failure Dogs

Sl. No	Days				
	Zero	3rd	7th	14th	28th
1	6.7	5.4	4.9	4.4	
2	9.9	9	8.7		
3	13.8	13.9	13.2	13.8	14
4	12	11.6	9.1	9	9.8
5	11.9	10.6	10.4	12.8	13
6	8.9	8.6	8.9	9.2	9.4
7	14.3	14.6	14.2	13.9	14.8
8	16.4	13.8	11.2	10.2	10.8
9	15.3	17	12.8	12.2	13.1
10	11.1	11	11.8	12	12.4
11	9.1	6.9	4.8		
12	8.7	8.4	7.8		
13	7.7	7.8	7.1	6.2	
14	11.8	11	7.8	5.9	
15	8.9	9	11.7		
16	10.4	10	8.3		
17	8.1	7.8	7.1		
18	10.5	10.3	7.8	7.3	
19	9.4	9.2	8.9	8.1	6.7
20	11.1	10.9	9.9	9	8.6
21	13.1	13.5	12.9		
22	8	7.7	9.5		
23	13.8	11	9.8	9.2	
24	6.7	6.4	5.6		
25	12.8	11.9	11	13.8	13
26	12.2	12.4	11.8	11.6	10.2
27	11.1	11	11.8	12.3	10.2
28	11.2	11.5	12.7	12	11.9
29	16.2	13	12.3	10.9	11.2
30	8.5	8.2	7.8	7.6	7.2
31	5.9	8.7	5.5	4.7	
32	7.6	7.2	6.8	6	5.8
33	8.6	8.2	7.3	4.9	
34	8.3	7.7	7.5	7.1	6.9
35	10	10	9.9	11.2	12.1
36	9.8	10.2	10.5	12	12.8
37	14.7	14.2	13.9	14	13.8
38	12.2	12	10.8	10.1	11.8
39	9.8	9.6	8.9	8	9.2
40	12.9	12.5	12.9	12	12.3

Appendix III: PCV (%) Values in Renal Failure Dogs

Sl. No	Days				
	Zero	3rd	7th	14th	28th
1	21	17.9	16.7	16	
2	30.2	27.9	26		
3	42.8	42.4	43.2	42.9	44.6
4	37	33	26.5	27	30
5	30	28	31	34	41
6	26	24	28	30	30.5
7	46.5	45	45	44.6	42.7
8	52	43.7	32.8	33.8	29.2
9	47.3	49	38.9	36.7	39.5
10	37.8	36.2	38.2	41	46
11	28.6	24	14		
12	27	26	24		
13	22.2	23.5	21.4		
14	37.5	34	31	25.3	
15	32	29.1	37.1		
16	30	29.2	24		
17	28	27	22		
18	29.8	28	26	25.3	
19	27.4	26.9	26.2	23.5	22
20	34.4	32.8	30.6	28.4	27.6
21	41.9	39	36		
22	28.6	28.9	35.8		
23	41.9	39	36	34.8	
24	22	21	19.2		
25	41	34	35.8	40.1	38.2
26	43.4	42.4	40.8	38.2	35.5
27	37.8	36.2	38.2	37	32
28	40.5	41.5	45.3	42	40.1
29	61.5	43.2	38	36.6	32
30	29.9	28	27	27.5	26.3
31	19.3	27	18.2	15.2	
32	46.4	45.3	42.2	38.4	37.3
33	27	26	21	17	
34	25.9	25.1	22.9	26.3	31
35	34.2	34.1	33.1	34.5	36
36	30.9	31.1	32	36.1	36
37	44.2	46.4	40.8	42.6	41
38	38	40.2	38	41	39.3
39	43.9	42.2	42.5	39	41.3
40	34.96	33.5	31.69	33.36	36.47

Appendix IV: Serum Creatinine (mg/dl) Values in Renal Failure Dogs

Sl. No	Days				
	Zero	3rd	7th	14th	28th
1	10.4	6.4	6.1	5.4	
2	8.6	16.6	18.8		
3	3.4	3.4	3.2	2.9	2.8
4	6.1	5.9	4.5	4.2	3.9
5	3.1	3.6	3.4	2.7	2.2
6	3.9	3.6	3.6	3.5	3.1
7	2.9	2	1.5	1.5	1.4
8	7.4	5.9	4.5	4.2	3.8
9	2.7	2.7	1.8	0.9	1.2
10	4.1	3.9	3.8	3.4	3.3
11	6.5	8.5	9.1		
12	6.7	6.9	11.2		
13	5	3.1	4.7	5.7	
14	3.4	3.8	4.6	8.3	
15	16	17	27.1		
16	9.8	10.3	14		
17	5.9	6.7	11		
18	3.7	4.1	5.6	10.1	
19	2.4	2.6	3.1	4.2	5.6
20	3.6	3.5	3.8	4.9	5.8
21	19	22.5	23.3		
22	5.7	17.2	20.8		
23	5.4	5.8	6.4	9.2	
24	17	16.5	19.6		
25	4.5	1.9	1.5	1.2	0.8
26	3.9	3.8	3.8	3.4	3.1
27	4.1	3.2	3.8	4.2	4.9
28	15.3	10.5	2.8	1.5	1.8
29	2.72	2.5	2.4	2	1.8
30	2.8	3.2	4.3	4.9	5.3
31	6.9	5.4	4.5	8.6	
32	9.8	10.6	9.4	8.9	7.6
33	3.2	2.6	2.5	2.5	
34	8.9	6.8	5.4	4.9	4.1
35	2.2	2.1	1.4	1.2	0.9
36	2.3	2.4	2.1	2.3	3.2
37	4.3	1.1	1.2	0.8	0.3
38	3.9	3.7	3.2	2.4	1.8
39	6.5	6.2	6	4.5	3.1
40	2.1	1.5	1.9	1.5	1.5

Appendix V: Blood Urea Nitrogen (mg/dl) Values in Renal Failure Dogs

Sl. No	Days				
	Zero	**3rd**	**7th**	**14th**	**28th**
1	123	89	85	76	37
2	120	180	220		
3	29	32	28	25	22
4	78	57	43	37	35
5	67	71	43	39	34
6	47	41	42	39	36
7	36	24.6	22	19	16
8	97	80	58	40.8	48.3
9	34	37	14	16	24
10	49.5	46	39	36	28
11	98.2	115	120		
12	91	95	156		
13	40	36	58	69	
14	41	54	71	96	
15	96	102	250		
16	120	135	198		
17	46.8	104	134		
18	49	61	78	140	
19	57	61	75	95	129
20	34	43	51	85	103.5
21	223	230	250		
22	67	130	123		
23	48	64	89	112	
24	137	150	210		
25	67	19	17	14	18
26	57	55	53	43	42
27	49.5	33.2	43	69	85
28	166	135	14.8	19	24
29	70.3	70	47	43	24
30	56.4	59	94.9	100.5	110
31	146	143	49	176	
32	132	141	96.3	94.8	
33	39.2	34.3	27	28	
34	110	89	56	49	35
35	25	22	19	13	10
36	63	84	58	60	64
37	49	23	14	10	5
38	62.3	48.4	44.6	38.8	34
39	112	101	80.5	48.4	43.4
40	43	42.5	48.6	44	42