ENDOSCOPIC EVALUATION OF
GASTROINTESTINAL
TRACT IN CANINE RENAL FAILURE

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The aim of this research project was to study the incidence, nature and complications of gastrointestinal disease in canine renal failure and to evaluate the efficiency of endoscopy in identifying the gastrointestinal complications in canine renal failure.

Ten apparently healthy dogs (Group I) were evaluated and normal values for hematology, Serum biochemistry, urinalysis, fecal occult blood test, nephrosonography and Gastroduodenoscopy. Thirty five dogs with renal failure were identified by detailed clinical examination, hematology, serum biochemistry, urinalysis, and nephrosonography. Further, the dogs with renal failure are allotted the following five groups Group II- mild azotemia (BUN<50 mg/ dl, n = 6), Group III moderate azotemia (BUN 50- 90 mg/ dl, n= 8), group IV severe azotemia ( BUN 90 – 140 mg/ dl, n = 8), Group V ( BUN . 140 mg/dl, n = 13). Gastroduodenoscopy, endoscopy guided gastric mucosal biopsy studies and isolation of Helicobacter spp were done in all five groups.

The study revealed higher incidence in Labrador Retrievers, German Shepherds and Spitz. Anorexia, vomiting, melena, halitosis and oral ulcers were common gastrointestinal signs. In Hematology non – regenerative anemia and neutrophilic leukocytosis was observed in severe and very severe groups. Gastroduodenoscopy revealed erosions in caudal esophagus, hyperemia of LES, erosions in fundus, ulcers in pylorus and duodenum. Histopathology of endoscopy guided mucosal biopsy revealed submucosal fibrosis, increased goblet cell activity, erosions and ulcers. Both gastroduodenoscopic and Histopathologic abnormalities of gastric mucosa varied with the level of azotemia. Endoscopy guided mucosal biopsy was found to be more efficient in diagnosing mucosal abnormalities in uremic gastropathy. The prevalence of Helicobacter spp was found to be 17.14 % in dogs with renal failure.

Key words: Endoscopy: Canine renal failure: Helicobacter spp.
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CHAPTER I
INTRODUCTION

Renal failure is a well-recognized cause of morbidity and mortality in geriatric dogs. Though it is not limited to any age, sex, or breed of dogs, it is more prevalent in aged animals and juvenile renal diseases was also reported (Chew et al; 1983; Brown et al; 1990, and Cook et al; 1993). Renal failure has been indicted to be associated with the development of gastrointestinal, neuromuscular, musculoskeletal, endocrinologic, cardiopulmonary, hemopoietic, and ophthalmic manifestations in dogs.

The gastrointestinal tract is most commonly affected in renal failure (Schulmann and Krawiec, 2000). Gastrointestinal disturbances are often the signs that most concern the owner and may be the reason the pet is presented to a veterinarian. The dramatic nature of gastrointestinal tract disturbances strongly affects an owner’s perception of pet’s quality of life.

Little or no work has been so for documented regarding the number of animals that exhibit gastrointestinal signs of disease and the extent of gastrointestinal damage in uremic dogs. Whereas, 40% of people with renal failure reportedly have gastrointestinal complications. Mucosal lesions of gastritis on endoscopic evaluation of human patients with renal failure (Krawiec, 1996).

Veterinary gastrointestinal endoscopy has evolved rapidly in past 20 years. Endoscopy is now considered an indispensable procedure in small animal veterinary
medicine, as it is a minimally invasive, atraumatic technique that permits visual examination of gastrointestinal lesions and allows descriptive or photographic documentation of their severity and extent. Further it also guide to acquire mucosal biopsy specimen for histopathological examination. Hence endoscopy may be useful in identifying the nature and severity of uremic gastropathy at different levels of azotemia.

Recently *Helicobacter spp* has been detected in stomachs of healthy dogs and dogs with signs of gastritis. (Happonen et al; 1998) and the role of *Helicobacter spp* in the pathogenesis of gastric disease in dogs is still debated. *Helicobacter pylori* has been linked to peptic ulcer disease, type B atrophic gastritis, gastric adenocarcinoma and gastric mucosa associated lymphoma (Strauss-Ayali and Simpson, 1999) *Helicobacter pylori* was also isolated in human patients with chronic renal failure (Shousha et al 1989; 1990 and Chhinna et al; 1998). Hence,a study on the incidence of *Helicobacter spp* in stomach of dogs with renal failure may be of interest.

Against the backdrop of the information’s cited; the present study was under taken with the following objectives.

1) To study the incidence of gastrointestinal complications in canine renal failure in this locality.

2) To study the nature of gastrointestinal disease and its complications in canine renal failure.

3) To evaluate the efficiency of endoscopy in identifying gastrointestinal complications in canine renal failure.
CHAPTER –II
REVIEW OF LITERATURE

2.1. RENAL FAILURE

The term 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 fluid, electrolyte and acid-base balances (DiBartola, 2000).

2.1.1 Terms and Concepts

Azotemia is an abnormal concentration of urea, creatinine, or other nonprotein nitrogenous substances in blood, plasma or serum and it may be categorized as pre renal, renal, post renal or combinations of these factors (Polzin and Osborne, 1995).

The term renal disease refers to the presence of morphologic or functional lesions in one or both kidneys, regardless of extent. (DiBartola, 2000)

‘Uremia’ is a term coined by Piorry and L’Heriter in 1840 (Baby, 1994). In current usage uremia refers to the constellation of clinical signs and biochemical abnormalities associated with a critical loss of functional nephrons and includes the extra renal manifestations of renal failure. (DiBartola, 2000).

Renal failure implies that two-thirds to three fourths or more of the functional capacity of both kidneys has been impaired. The term often is used to connote a less severe state of renal dysfunction that is not (yet) associated with polysystemic clinical manifestations (Polzin and Osborne, 1995).
2.2.RENAL FAILURE IN DOGS

Kirk et al. (1968) stated that renal disorders were the most common diseases of the dog and majority of old dogs have suffered some degree of kidney damage. Renal disease is one of the most common disorders of dogs and uremia is common sequel of any renal malfunction (Tabotabo et al., 1970 and Murray et al., 1971).

2.2.1. Incidence

Renal failure is not limited to any age, sex, or breed of the dog but is more prevalent in aged animals. In 170 dogs with renal failure presented to the Veterinary Medical Teaching Hospital of the University of California for a five-year period, their mean age was 6.95 years (Cowgill and Spangler, 1981). Earlier, Richards and Hoe (1967) reported the mean age as 6.5 years in a review of 119 canine cases. Though the incidence is more in geriatric dogs, juvenile nephropathies were also reported in recent literature.

Polzin et al., (1995) stated that eighteen per cent of dogs with renal failure were younger than 4 years, seventeen per cent between 4 to 10 years, twenty per cent between 7 to 10 years and forty five per cent older than 10 years.

Low (1981) reported 1.8 per cent and Doxey (1983) reported 1.1 per cent as the incidence of renal disease in dogs in hospital admissions.

Akshay (2000) reported that the incidence of renal disease was 0.37 per cent in dogs presented to Madras Veterinary College Hospital during 1999 – 2000.
2.2.2. Clinical signs

Watson (1977) stated that the predominant signs in compensated renal failure were polyuria and polydipsia, uremia develops when the owner overlook these signs.

Kelly (1979) reported depression, muscular weakness, laboured respiration, oliguria or anuria, loss of body condition, dehydration, anorexia, vomiting, hyperemic mucous membrane, ulceration in buccal mucosa, coma and death as the clinical signs of uremia.

In acute renal disease the onset of clinical signs will be abrupt and these signs include anorexia, depression, vomiting and thirst. The rectal temperature was often normal, but an arched back, stiff joint and lumbar pain may be encountered. In chronic cases the signs were progressively increasing thirst, polyuria, and loss of bodyweight. Anorexia, vomiting, and halitosis will be observed in more advanced cases (Doxey, 1983).

2.2.3. Hematology

McIntyre (1954) noted the presence of anemia in 57 per cent of animals with chronic renal failure and in 20 per cent of animals suffering from the most severe form of the primary renal failure.

Naets (1963) demonstrated a relationship between renal failure, anemia and uremia in nephrectomised dogs.

Bentinck-Smith (1969) presented the normal hematological values in dogs as, Hemoglobin 12-18 (15) g per cent; packed cell volume 37-55 (45) per cent; total erythrocytes 5.5 – 8.5 (6.8) million/cu.mm; total leucocytes 6000-17000/cu.mm; eosinophils 100-1250 (550)/cu.mm; monocytes 150 – 1350 (750)/cu.mm and lymphocytes 1000 – 4800 (2800)/cu.mm.
Several authors often observe a nonregenerative normocytic normochromic anemia in chronic renal failure (Osborne et al., 1972; Schalm et al., 1975 and Finco, 1980). Mc Caw et al., (1989) opined that renal failure accompanied by neutrophilia with left shift was suggestive of pyelonephritis.

2.2.4. Serum biochemical profile

2.2.4.1. Serum urea nitrogen and creatinine

Kaneko (1980) and Coles (1983) reported the normal blood urea levels as 10-28 mg/dl and 10-20 mg/dl respectively. Osborne et al., (1972) opined that BUN values exceeding 45 mg/dl indicate diminishing glomerular filtration rate.

Jackson (1964) opined that BUN and creatinine were the best indices of the amount of toxic products retained in the body due to impaired renal function and stated that the normal creatinine value for dogs as 1-2 mg/dl ,while a level of 2-5 mg/dl was indicative of guarded prognosis, 5-7 mg/dl poor prognosis and above 7mg/dl an unfavorable prognosis.

Plasma creatinine values in the normal dog fall within the range of 1.0 –2.0 mg/dl. Creatinine levels of 4 to 5 mg/dl were considered indicative of serious renal damage and levels above 7.5 mg/dl were critical (Richards and Hoe, 1967).

Finco and Duncan (1976) reported the elevated mean BUN values of 89 ± 11.8 mg/dl, 140 ± 11.6 mg/dl and 194 ± 15.3 mg/dl and mean serum creatinine values of 2.4 ± 0.4 mg/dl, 4.9 ± 0.3 mg/dl, and 9.1 ± 1.2 mg/dl, in prerenal, renal and post renal uremia in dogs.

According to Doxey (1983) elevated blood urea levels above 10 m.mol/L should be regarded as indicative of some impairment of renal function levels above 20 m.mol/L was considered serious and above 50 m.mol/L was extremely serious. He also stated that high blood urea levels can also occur in dehydrated animals.
Chew and DiBartola (1986) demonstrated the relationship of blood urea nitrogen (BUN) and serum creatinine concentrations to the percentage of functional nephrons.

2.2.4.2. Total protein and albumin

A reduced serum protein level occurs in wide variety of diseases including glomerulonephritis, amyloidosis and nephrosis due to urinary protein loss (Wiseman et al., 1980). Hall (1983) opined that a low serum protein level in the absence of urinary protein loss may result from variety of non-renal diseases. The normal serum total protein level in animals is 5.7 – 7.6 g/dl (Dibartola, 1986).

The albumin/globulin ratios in most domestic species is 0.5 to 1.50 although lower values, have been observed in apparently healthy animals. Hypoalbuminemia is known to occur in glomerulonephritis, amyloidosis and occasionally in interstitial nephritis, malnutrition, parasitic diarrhea and hepatic pathology (Kronfeld and Medway, 1969).

Benjamin (1985) suggested that hypoalbuminemia might result from inhibition of synthesis, increased protein catabolism from stress, leakage of albumin through damaged vessels and tissues and secondary to increased globulin concentration.

2.2.4.3. Serum potassium and phosphorus

Coutler and Engen (1972) reported that the normal serum potassium of healthy dogs as 3.5 ± 0.2 m Eq/L.

Kaneko (1980) observed the normal potassium levels in serum of healthy dogs ranges from 3.7 to 5.8 mEq/L. DiBartola (1985) recorded hyperkalemia (5.6 –8.9 mEq/L) in acute renal failure due to ethylene glycol ingestion.

In cats with urinary obstruction metabolic acidosis, mild hypematremia, hyperkalemia, hypermagnesemia, hypercalcemia, hyperphosphatemia and
hypoproteinemia were usually accompanied the azotemia. In dogs hyperkalemia, marked hyponatremia, hypochloremia and compensated metabolic acidosis were reported in rupture of urinary bladder (Finco and Cornelius, 1977; Burrows and Bovee, 1978).

2.2.5. Urinalysis

Abnormalities in the urine only indicate the presence of kidney damage but do not provide any quantitative measure of the extent of damage (Jackson, 1964).

Osborne et al., (1972) stated that the presence of significant numbers of casts localized the disease process to the kidneys and their type may indicate the significant damage to distal tubules and collecting ducts.

Coles (1986) stated that microscopic examination of urine samples is of clinical importance and should never be omitted from routine urinalysis. Bush (1992) reported that urine samples contain WBC casts and RBC casts in pyelonephritis cases.

2.2.6. Fecal occult blood test

Writh (1956) stated that the feces of carnivores give false positive reaction to the occult blood test, unless treatment is withheld for proceeding 2-3 days. Burrows (1986) opined that melena might be observed if bleeding is severe in peptic ulceration in dogs.

Willard (1992) opined that the blood may not get distributed homogenously throughout the fecal mass and hence in such cases, a negative reaction is likely to occur.

2.3. NEPHROSONOGRAPHY

Wood and McCarthy (1990) opined that in clinical Veterinary medicine, Ultrasonographic imaging of the kidney was of major importance in diagnosis of renal diseases.
Konde et al. (1986) reported that the ultrasonography appeared to be more sensitive method than survey radiography and excretory urography in differentiating the internal characteristics of renal lesions.

Reported risks associated with excretory urography like contrast medium induced nausea, vomiting and contrast medium induced renal failure could be avoided by ultrasonography (Feeney et al., 1980; Heritage and Dennis, 1987 and Daley et al., 1994).

Sonography provides anatomic information in patients with impaired renal function in situations where urography is contraindicated (Johnston et al., 1986 and Walter et al., 1987).

Felkai et al. (1995) stated that the sonography is less invasive than pyelography and should be used if there is a suspicion of abnormalities of renal pelvis and proximal ureter.

2.3.1. Nephrosonographic technique

Nyland et al. (1989) opined that the non-invasive calculation of the kidney volume using sonography was accurate when used serially on the same patient to detect disease progression. Konde et al. (1986) obtained static B-mode nephrosonograms with a 3.5 or 5.0 MHz transducer positioned to image the kidney in sagittal and transverse planes.

Walter et al. (1987) performed ultrasonographic examinations in 32 dogs by use of sector and/or static B-mode scanner. All ultrasonograms were made with the dog in dorsal recumbency. Sagittal renal scanning began at the medial aspect of the kidney and proceeded laterally, usually at 0.5 cm intervals if performed with static B-mode scan. Transverse renal scanning began at the cranial pole and proceeded caudally.
Barr (1990) made nephrosonographic examination by placing the dog in lateral recumbency. Coronal and transverse sectional views were obtained using 3.5 to 5.0 mHz mechanical sector transducers.

Nephrosonographic examination may be performed in either dorsal or lateral recumbency. Preparation requires clipping the hair over the entire abdomen, including midway up the body wall over the right and left caudal intercostal spaces. Use liberal amounts of acoustic coupling gel to provide sufficient contact. A linear or sector transducer may be used. For medium to large breed dogs a 5 to 7.5 mHz transducer is recommended. A 7.5 to 10 mHz recommended in small dogs and cats. It is important to apply firm pressure with the transducer to gain maximal contact and to displace overlying bowel gas (Nyland et al., 1995).

In dogs left kidney is caudal to greater curvature of stomach, caudodorsal to the spleen, lateral to the aorta and left adrenal gland and is about at the level of L2 to L4 vertebrae. The right kidney is caudal to right liver lobes, lateral to caudal venacava and right adrenal gland and is generally more cranial than left kidney at about the level of L1 to L3 vertebrae. (Nyland et al., 1995). Because of the right kidney’s cranial position in dogs, it is often necessary to image the right kidney through eleventh and twelth intercostals spaces (Armbrust et al., 2001).

Three imaging planes can be used, the dorsal, sagittal and transverse planes obtained with transducer placed at lateral, ventral and lateral/ventral windows respectively (Armbrust et al., 2001).

2.3.2. Normal nephrosonographic anatomy

Familiarity with the normal ultrasonographic appearance of the canine kidney is mandatory for differentiation of normal from abnormal ultrasonographic anatomy
The normal ultrasonographic anatomy of the canine kidney has been described (Konde et al., 1984 and Konde, 1985)

In sagittal plane, structures consistently visualized are the capsule, renal sinus, renal crest (renal pyramid or renal papilla), medulla, cortex and pelvic diverticuli (Wood and McCarthy, 1990). The hypo echoic medulla and an outer zone of intermediate echogenicity corresponding to the renal cortex surround the renal sinus. The arcuate and intralobar vessels are sometimes seen as discrete echogenicities at the corticomedullary junction (Nyland et al., 1995).

Normally, an anechoic space should not be identified in the renal pelvis, diverticuli or ureters. Occasionally, a mild degree of pelvic dilatation during intravenous fluid administration has been noted in normal canine kidneys (Felkai et al., 1995).

Compare the echogenicity of kidney cortex with that of the spleen on the left and 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. The renal cortex is hyper echoic relative to the medulla. The renal sinus is the most hyper echoic because of highly reflective interfaces of fat and fibrous elements of the vasculature and pelvic diverticuli (Nyland et al., 1995).

The normal ultrasonographic kidney dimensions in cats have been reported to range from 3 to 4.3 cm in length, 2 to 3 cm in width and 1.8 to 2.6 cm in height (Armbrust et al., 2001).

There is no established value for kidney size or volume in dogs, although corrections between body weight and kidney size and volume have been attempted (Barr, 1990; Barr et al., 1990). The renal volume can be determined by using the formula for an ellipsoid \( V = L \times W \times d \times 0.523 \). with this technique, the estimated
volume tends to be lower than the actual volume. A significant tendency to under estimate length has also been identified. (Barr, 1990). However they are not routinely used except to assess acute allograft rejection in renal transplant patients (Armbrust et al., 2001).

2.3.3. Abnormal nephrosonographic findings

2.3.3.1. Diffuse parenchymal abnormalities

Grooters and Biller (1995) stated that the hyperechogenicity of renal cortex and the medullary rim sign are the two common sonographic findings in the diffuse parenchymal diseases. Hyperechogenicity of renal cortex is nonspecific and it can occur in number of infiltrative, inflammatory, degenerative disorders and also be produced artifactually. The rim sign has been observed in ethylene glycol toxicosis, hypercalcemic nephropathy, pyogranulomatous nephritis, acute tubular necrosis and severe chronic interstitial nephritis.

2.3.3.2. Interstitial nephritis and glomerulonephritis

Ultrasonographic abnormalities associated with glomerulo/interstitial nephritis include mild to moderate cortical hyperechogenicity and decreased corticomedullary demarcation (Nyland et al., 1995). A normal ultrasonographic examination does not entirely rule out renal disease (Walter et al., 1987).

2.3.3.3. Hypercalcemic nephropathy

Renal ultrasonographic findings in dogs with hypercalcemic nephropathy include increased cortical echogenicity and the presence of hyper echoic rim at the corticomedullary junction (Armbrust et al., 2001).
2.3.3.4. Focal parenchymal abnormalities

Walter et al., (1987) reported focal or diffuse lesions with complex echogenicity and anatomic disruption, although not specific for cell type, appeared to be a common finding in renal neoplastic invasion.

Renal cysts are typically sonolucent and have smooth internal walls and prominent distant enhancement (Armbrust et al., 2001).

2.3.3.5. Renal collecting system abnormalities

Felkai et al., (1995) stated that the two most common lesions associated with the renal pelvis are hydronephrosis and nephrolithiasis.

2.4. COMPLICATIONS OF CANINE RENAL FAILURE

May et al., (1987) opined that the diverse clinical and laboratory findings characteristic of uremia and emphasized its association with impairment of one or more fundamental cell functions.

Polzin and Osborne (1995) recorded the gastrointestinal, neuromuscular, musculoskeletal, endocrinologic, cardiopulmonary, hemopoietic and ophthalmic manifestations in uremic syndrome in dogs.

Rubin (1995) stated that the uremic syndrome includes many metabolic and endocrinologic disturbances that arise through loss of homeostatic, synthetic and catabolic functions of the kidney as well as abnormalities arising from renal compensatory mechanisms and the presence of extra renal manifestations (e.g. Hemorrhagic gastroenteritis, anemia, osteodystrophy, coagulopathies) is usually implied when the patient is described as uremic.

Systemic hypertension is now recognized as being commonly associated with renal disease in humans and animals. Though primary hypertension may cause renal disease in some people, in others the increase in blood pressure is the result of
primary renal disease (Kobayashi et al., 1990). Systemic hypertension has been reported in 50 to 93 per cent of dogs with renal failure, approximately 85 per cent of dogs with glomerular disease may be hypertensive (Cowgill and Kallet, 1986).

Bartges et al., (1996) reported that the pathologic ophthalmic findings like retinal arteriolar tortuosity, perivasculitis, papilledema, retinal edema and detachment and retinal and vitreal hemorrhage as the common clinical consequences of systemic hypertension in humans, dogs and cats.

Rubin (1997) stated that the nervous system abnormalities associated with uremia may include dullness, lethargy, tremors, gait abnormalities, myoclonus, seizures, stupor and coma and opined that these signs may be due to the effects of uremia or hyperparathyroidism.

Non regenerative anemia secondary to erythropoietin deficiency is an invariable consequence of chronic renal failure in companion animals (Cowgill, 1995), but its significance remained poorly characterized and its management was ignored until the recent development of recombinant human erythropoietin (King et al., 1992). The pathogenesis of this anemia is multifactorial but erythropoietic failure of bone marrow secondary to inadequate renal production of erythropoietin is regarded as the primary cause (Cowgill et al., 1998).

Metabolic acidosis is estimated to occur in two thirds to three fourths of dogs and cats with renal failure. It is caused by limited ability of surviving nephrons to excrete hydrogen ions. Consequences of metabolic acidosis associated with renal failure include anorexia, nausea, vomiting, weight loss, lethargy, intolerance to dietary acids, hypokalemia, muscle weakness, bone demineralization and possibly progression of renal failure (Osborne et al., 1995).
A complication of CRF is the development of secondary hyperparathyroidism, which is the result of factors such as phosphorus retention, hypocalcemia, calcitriol deficiency and parathyroid hormone resistance of bone (Bover et al., 1994). Dogs with chronic renal failure have parathyroid gland hyperplasia (Capen, 1993). Ultrasonographic examination of parathyroid glands was found to be useful and in differentiating acute renal failure and chronic renal failure in dogs with severe azotemia (Reusch et al., 2000).

### 2.5. GASTROINTESTINAL COMPLICATIONS IN CANINE RENAL FAILURE

Gastrointestinal complications, among the most common and prominent clinical effects of uremia, include stomatitis, gastroduodenitis, enterocolitis and associated clinical signs of anorexia, nausea, vomiting and diarrhea (Polzin and Osborne, 1995).

Rubin (1997) stated that the gastrointestinal complications are some of the most common and notable clinical signs of uremia.

Krawiec (1996) reported that the dogs and cats with uremia might display abnormalities of essentially all parts of the gastrointestinal tract. Clinical signs of gastrointestinal complications of uremia may include anorexia, nausea, vomiting, abdominal pain, diarrhea and gastrointestinal bleeding.

No data exists indicating the number of uremic animals that exhibit gastrointestinal signs of disease, but 40% of people with renal failure reportedly have gastrointestinal complications. Mucosal lesions of gastritis and duodenitis are most commonly seen on endoscopic evaluation of human patients with renal failure (Krawiec, 1996).
Shousha et al., (1989) reported 59% incidence of chronic duodenitis and 62.5% incidence of gastric metaplasia in human patients with chronic renal failure.

Krawiec (1996) stated that the dogs and cats with uremia display abnormalities of essentially all parts of gastrointestinal tract. Gastrointestinal complications of uremia includes uremic breath, stomatitis, oral ulceration, parotiditis, anorexia, nausea, vomiting oral or gastrointestinal hemorrhage, gastrointestinal perforation, diarrhea, constipation, intestinal obstruction and pseudomembranous colitis, which may result from inflammation, edema, erosions, ulcerations and/or necrosis.

2.5.1. Clinical signs of gastrointestinal complications

Chhina et al., (1998) stated that upper gastrointestinal tract symptoms including anorexia, nausea, vomiting, epigastric pain and heart burn as common manifestations of uremia in human patients. Franzin et al., (1982) reported nausea, vomiting and epigastric pain occurring separately or in various combinations in 37 per cent of human patients with chronic renal failure.

Krawiec (1996) opined that the clinical signs of gastrointestinal complications of uremia may include anorexia, nausea, vomiting, abdominal pain, diarrhea and gastrointestinal bleeding.

2.5.1.1. Anorexia

Rubin (1997) stated that the anorexia might initially manifest as selective appetite with preferences developing for certain usually more palatable foods with these preferences may wax and wane. The inappetance progress to complete refusal of all food. Schulman and Krawiec (2000) opined that anorexia occurs for a variety of reasons like polyuria, polydipsia, hypokalemia, metabolic acidosis, nonregenerative
anemia, hypergastrinemia, secondary hyperparathyroidism, uremic toxins, gastric hyperacidity etc.

2.5.1.2. Weight loss

Weight loss may be caused by physiologic abnormalities as well as anorexia induced inadequate caloric intake. Chronic renal failure results in metabolic acidosis, which in turn promotes a state of protein malnutrition by increasing the rate of protein catabolism (Bergstrom, 1995). This proteolysis is in addition to the impaired insulin stimulated protein synthesis found in uremic patients (Polzin et al., 1995). Weight loss may also reflect a low grade malabsorptive syndrome resulting from uremic gastroenteritis and other potential causes of weight loss includes vaguely defined uremic toxins, especially guanidine compounds (Chew and DiBartola, 1989).

2.5.1.3. Vomiting

Vomiting a frequent complaint in renal failure occurs due to hypokalemia, acidosis, uremic gastroenteritis and from the effects of uremic toxins on chemo receptor trigger zone (Schulman and Krawiec, 2000). Vomiting may not occur until the later stages of chronic renal failure and the severity of vomiting varied with the degree of azotemia (Rubin, 1997).

2.5.1.4. Stomatitis

Krawiec (1996) reported that the uriniferous / ammoniacal breath, stomatitis and mouth ulcers are the common oral signs of uremia. The conversion of salivary urea into ammonia by urease-producing bacteria may be responsible for the mouth lesions (Doherty, 1992).

Oral ulcerations typically seen on buccal mucosa and tongue. Brownish discoloration with necrosis and sloughing of anterior portion of tongue as a result of fibrinoid arteritis and focal ischemia (Schulman and Krawiec, 2000). Xerostomia and
sialorrhea are also seen in uremic dogs and cats (Valenzuela, 1983). These problems are exacerbated by the poor oral hygiene typical in veterinary patients.

2.5.1.5. Uremic gastroenteritis

Anatomic and functional abnormalities have been identified at all levels of gastrointestinal tract in uremic animals. Gross anatomic abnormalities include gastritis, ulceration and hemorrhage (Lazarus, 1991). Microscopic changes include glandular atrophy, edema of lamina propria, mast cell infiltration, fibroplasias, mineralization and submucosal arteritis (Osborne and Polzin, 1995). Functional abnormalities include abnormalities in acid-pepsin secretion, gastric emptying, mucosal permeability and serum gastrin levels (Doherty, 1992).

Gastrin is cleared by the kidneys and therefore accumulates in renal failure. The hypergastrinemia stimulates the parietal cells to release more hydrochloric acid. Back diffusion of acid and pepsin through stomach wall creating infiltration and hemorrhage, which stimulates mast cells to release histamine. This histamine then stimulates parietal cells to release more hydrochloric acid. Thinning of protective mucous layer in stomach further increases the back diffusion of hydrochloric acid. Ischemias due to vascular lesions also complicate gastroenteritis (Osborne and Polzin, 1995).

The mechanism of hypergastrinemia is controversial (Lichtenberger et al., 1993). Pentagastrin-stimulated acid output was found to be greater in rats with induced renal failure than normal rats (Quintero and Guth, 1992).

Some authors had claimed that chronic renal failure is associated with hypochlorhydria (Paimela, 1985; Ala-Kailia et al., 1987 and Bredt and Snyder, 1990), while others have reported normal or high acid secretion (Venkateswaran et al., 1972; Shepherd et al., 1973 and Sullivan et al., 1976). A possible mechanism for normal or
decreased gastric acidity in uremia is neutralization of gastric acid by elevated concentrations of ammonium ion in gastric fluids due to the action of bacterial urease on gastric urea (Polzin and Osborne, 1995). In humans, *Helicobacter pylori* infection has been associated with increased gastric ammonia levels in uremia, although the presence of this bacterium does not correlate with clinical signs (Triebling *et al*., 1991 and Kang, 1993).

Renal failure has been suggested to interfere with the normal mucosal barrier, increased proton permeability and enhanced susceptibility to acid injury (Quintero *et al*., 1992). Polzin and Osborne (1995) implicated other factors in the genesis of uremic gastropathy such as psychological stress, proton back-diffusion by high urea levels, ammonia liberated by bacterial urease, decreased concentration and turnover of gastric mucus and pyloric incompetence.

Doherty (1992) noted the motility disorders including delayed gastric emptying and gastroesophageal reflux in humans with chronic renal failure and opined that these may result from electrolyte alterations, disturbances in gastrointestinal hormones or autonomic nervous system dysfunction.

**2.6. GASTRODUODENOSCOPY**

**2.6.1. Endoscopy in canine practice**

Bonneau and Reed (1972) described the use of gastrocamera in dogs. Amis and McKiernan (1986) stated that the flexible fibreroptic endoscope was first introduced by Ikeda in 1967.

Ament *et al*., (1988) stated that the upper gastrointestinal endoscopy is a safe and sensitive method for diagnosis of upper gastrointestinal diseases. Obrien (1980) stated that gastroscopy can detect gastritis which is not detectable by radiology and
thus, the endoscopy greatly contributes to an understanding of the pathogenesis, incidence and management of gastritis in small animals.

Strombeck (1983) opined that endoscopic examination of stomach is not useful for detection of motility disorders but it remained a sensitive method in detecting mucosal disorders.

Tams (1992) concluded that the endoscopy is reliable than contrast radiography in the diagnosis of gastric erosions, ulcerations, chronic gastritis, gastric neoplasia and inflammatory bowel disease.

Simpson (1993) opined that endoscope used for gastrointestinal tract examination of dog and cat generally had a working shaft length of at least 1 M, outside diameters of 7.9 – 9.8 mm and a flexible maneuverable tip capable of four way deflection with wide field of view (≥100°).

Denovo (1995) suggested the important considerations in selecting a gastrointestinal endoscope.

2.6.2. Preparation and restraint of patient

Tams (1990) revealed that the stomach should be empty for successful gastroscopy. No food should be given for 12 – 18 hours and water should be withheld for 4 or more hours before examination.

Ritcher (1992) suggested that though a fast of 12 – 24 hours is necessary to prevent food in the stomach, when there is evidence of delayed gastric emptying, a longer fast may become necessary.

General anesthesia is required for gastroduodenoscopy. Atropine and other anticholinergic drugs are not used unless required to increase heart rate as these drugs alter gastric motility and increases the pyloric tone (Tams, 1990).
Tams (1990) suggested that the patient should always be placed on left lateral recumbency. The antrum and pylorus are away from tabletop in this position, which improved the endoscopist’s ability to completely examine and readily traverse these structures with the endoscope.

2.6.3. Gastroduodenoscopic technique

2.6.3.1. Esophagus

Guffy (1979) demonstrated the need of general anesthesia and tracheal intubation before esophagoscopy and further advocated the use of lubricated esophagoscope, which is passed dorsal to trachea into esophageal lumen.

In case of dogs, the cervical lumen of the esophagus was narrower than the thoracic esophagus and the intubated trachea can be seen pushing into the lumen. The esophageal mucosal color is pale gray/pink and cardia is generally set at an angle to the long axis of esophagus.

Tams (1990) stated that the entrance to the upper esophageal sphincter is actually dorsal to the larynx and once the endoscope is passed through the upper esophageal sphincter, there is usually a little resistance and the instrument can easily be advanced into the lumen. The cervical part of the esophagus is always collapsed and in dogs it has the appearance of pliant, longitudinal folds and insufflation by air distends the wall of the esophagus and hence there is easy visualization of the mucosa and the lumen of the esophagus. The aortic indentation and pulsations of heart can be viewed as endoscope is advanced over the base of the heart.

Ritcher (1992) suggested that the normal glistening esophagus is pale pink and fine submucosal vessels are easily visualized and lower esophageal sphincter is closed has a irregular rosette appearance.
2.6.3.2. Stomach

Tams (1990) stressed the importance of complete examination of every patient undergoing gastroscopy and described the detailed examination of stomach in canine patients.

2.6.3.2.1 Gastroesophageal junction

As the endoscope is advanced to the distal esophagus, the position and configuration of gastroesophageal junction are noted. Because the esophagus is essentially in a posterior plane compared with the location of the stomach, the endoscope tip should be deflected to the left approximately 30 degrees with simultaneous slight upward deflection as the gastroesophageal junction is passed. In some patients minimal or no upward deflection is needed. When properly directed there should be no resistance to advancing the endoscope to the stomach. If the endoscope tip is advanced too far before deflection begins, the endoscope should be retracted and repositioned.

2.6.3.2.2. Proximal stomach and gastric body

The endoscope tip should be positioned just through the gastroesophageal junction so that an overview and orientation within the gastric lumen can be obtained. As the tip enters the stomach, the rugal folds, generally on the greater curvature of the body will be seen. Often the stomach walls will be partially or completely collapsed. In this instance the view of the stomach will be quite limited and it is necessary to pause and insufflate air, at least to the point that the rugal folds begin to separate. This allows for spatial orientation and identification of most gross abnormalities. During insufflation the endoscopist must be careful not to cause over distension of stomach since this may result in significant cardiopulmonary compromise. When the stomach
is over distended the rugal folds will be almost completely flattened or not detectable, superficial blood vessels can sometimes be observed and there may be mucosal blanching.

Several observations should be made during initial examination of the stomach. These include presence of any fluid or ingesta, ease of distensibility of gastric walls and gross appearance of rugal folds and mucosa.

As the endoscope is gradually advanced through the proximal stomach, the area of the gastric body can be thoroughly evaluated by using the control knobs to deflect the endoscope tip or by rotating the insertion tube with the right hand. With the patient in left lateral recumbency and endoscope held in a conventional manner the smooth lesser curvature is an endoscopist’s right and the rugal folds of greater curvature are seen below and to the left. The endoscope is advanced along the greater curvature until angulus is identified. The angulus appears as a large fold extending from lesser curvature. The angulus is an important landmark that separates the body of the stomach from the antrum.

Once the angulus and antrum are reached, the endoscopist has the option of advancing directly through the pyloric canal to the duodenum or if completing the gastric examination. It is better to perform at least a cursory examination of the entire stomach before proceeding to the duodenum. A final move through gastric examination and procurement of biopsies are usually done after duodenoscopy.

2.6.3.2.3. Retroversion (J-maneuver)

Retroversion maneuver provides an enface view of the angulus, cardia and fundus. To provide an enface view of the angulus; the retroversion maneuver must be initiated at the point opposite to angulus. The endoscope is advanced along the greater curvature to the level of the distal body and proximal antrum. The inner control knob
is turned counter clockwise as the endoscope is gradually advanced, the angulus can
be seen enface. The endoscope tip is deflected upward as far as possible and advanced
further. This provides a view of cardia. Pulling the endoscope back draws the tip
closer to the cardia. Air insufflation is necessary to keep proximal stomach dilated.

The tip can be advanced to the proximal antrum while still in retroflexed
configuration. When the angulus comes into view, the deflection knobs are returned to
a neutral position. The antrum and pylorus are then in view.

2.6.3.2.4. Antrum

The antrum differs from the body of the stomach in that there are no rugal
folds and peristaltic contractions are sometimes observed in the antrum. To advance
from the distal body to the antrum, upward deflection is applied as the instrument tip
is passed along the distal greater curvature. From this position the endoscopist can
appreciate the appearance of two separate “tunnels”. The upper area is the gastric
body and the more dependent funnel is the antrum.

2.6.3.2.5. Pylorus

In most animals the pylorus can be easily identified as the endoscope is
advanced through the antrum. Variable degrees of dilation of the pyloric canal will be
observed. In some cases the pylorus will be persistently closed and occasionally the
exact location of pyloric opening will be quite difficult to identify. The cardinal rule
in successfully advancing the endoscope through pylorus is to keep the pylorus in the
center of the endoscope field. Because the pyloric position commonly changes
slightly every time the patient breathes, small adjustments of the up/down deflection
knob and minor insertional tube rotational changes will be required as the endoscope
tip is gradually advanced towards the pylorus.
2.6.3.3. Duodenum

Obrien (1980) opined that once the pyloric sphincter is passed during gasteroduodenoscopy, advancement of the tip of the endoscope is carried out quickly to the flexure joining descending and ascending duodenum. Only the descending duodenum is usually examined because there are few indications for examining the ascending duodenum. The duodenal mucosa normally appears velvety or shaggy because of the presence of villi.

Major and minor duodenal papillae and aggregated lymphatic nodules (Payer's patches) can be routinely identified in descending duodenum (Tams, 1990). Ritchter (1992) stated that the entry into the duodenum was relatively easy with practice if the pylorus is open and the normal duodenum in dogs was pink, smooth and uniform with friable duodenal villi.

2.6.4. Gastroduodenoscopic findings in renal failure patients

Gross anatomic abnormalities including gastritis, ulceration and hemorrhage, microscopic changes include glandular atrophy, edema of lamina propria, mast cell infiltration, fibroplasias, mineralization and submucosal arteritis had been reported by several authors in uremic dogs (Lazarus, 1991; Polzin and Osborne, 1995; Krawiec, 1996; Schulman and Krawiec, 2000) and Kavitha (1997) recorded hemorrhagic type of ulcerative gastritis endoscopically in uremic dogs.

No data has been published indicating the number of uremic animals that exhibit gastroduodenoscopic abnormalities.

2.6.4. Endoscopy guided gastric biopsy

Sinclair et al., (1978) stressed the importance of histopathological examination of gastroscopic biopsy material in making a definitive diagnosis. Happe et al., (1981) reported that biopsies taken near the pylorus were two small and superficial for adequate histological examination.
Sullivan and Miller (1985) stressed the need of tissue sample for histopathological examination in cases that appear endoscopically normal. Ettinger (1989) stated that uremic gastropathy is accompanied by glandular atrophy, edema of lamina propria, mast cell infiltration, fibroplasia, submucosal arteritis and erosive changes.

Similarly microscopic changes like glandular atrophy, edema of lamina propria, mast cell infiltration, fibroplasias, mineralization and submucosal arteritis has been reported by several authors (Lazarus, 1991; Polzin and Osborne, 1995; Krawiec, 1996; Schulman and Krawiec, 2000).

2.7. HELICOBACTER ASSOCIATED GASTRIC DISEASE IN DOGS

The first gastric spiral organisms in humans were described by Bottcher in 1974 and were described in animals by Rappin in 1881 (Bizzozero, 1893). In 1896, Salomon observed spiral organisms in canine, feline and brown Norway rat stomachs (Strauss-Ayali and Simpson, 1999). These studies illustrated that bacteria can densely colonize the euhlorhydric stomach, which was traditionally considered to be predominantly sterile.

These gastric spiral organisms once named as Campylobacter jejuni was later renamed as Helicobacter pylori. H. pylori is now known to colonize the stomachs of 20 per cent to 95 per cent of healthy adult human populations world wide and is associated with persistent, active, chronic gastritis, peptic ulcer disease, gastric adenocarcinoma and gastric mucosa associated lymphoma (Strauss-Ayali and Simpson, 1999). Helicobacter like organisms (HLOs) were isolated from the stomachs of ferrets, nonhuman primates, dogs, cats, pigs and cheetahs and were shown to belong to the new Helicobacter genus.
2.7.1. Species characteristics

*Helicobacter spp* are gram-negative, microaerophilic, curved to spiral-shaped bacteria. *Helicobacter* includes 14 formally named species as well as other unnamed closely related organisms (Fox, 1998). All of these are urease and catalase positive. All canine gastric *Helicobacter spp.* are relatively similar in length (5 – 15 µm) and width (0.3 – 1.2 µm), which prevents their designation by light microscopy (Jalava et al., 1997). Speciation can be done by 16sRNA sequencing, DNA hybridization, electron microscopy and highly standardized sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS PAGE) (Eaton et al., 1996 and Jalava et al., 1998).

2.7.2. Prevalance

Fox (1995) stated that the prevalence of *H. pylori* varied between 20 to 90 per cent in human adult population worldwide.

Gastric *Helicobacter spp.* are highly prevalent in dogs and have been identified in 61 per cent to 82 per cent of dogs presented for the investigation of vomiting, in 67 per cent to 86 per cent of clinically healthy pet dogs (Strauss-Ayali and Simpson, 1999) and approaching 100 per cent in laboratory Beagles and shelter dogs (Cornetta et al., 1998). In a recent study of *Helicobacter* infected dogs, *H. bizzozeronii*, *H. felis*, *H. salomonis* and *F. rappini* are isolated in 55.6 per cent, 22.2 per cent, 22.2 per cent and 4.4 per cent of dogs respectively (Strauss-Ayali and Simpson, 1999).

Simultaneous infection with more than one species seems to be common and mixed cultures were grown from 8.6 per cent of biopsies from 48 infected dog (Jalava et al., 1998)
2.7.3. Pathogenicity

Gastric *Helicobacter spp.* has been suspected of inducing histologically verifiable gastritis, degeneration of the gastric glands and parietal cells (Henry *et al.*, 1987; Geyer *et al.*, 1993 and Hermanns *et al.*, 1995). However, such changes have been detected both in dogs suffering from gastrointestinal signs and in clinically healthy dogs (Henry *et al.*, 1987; Geyer *et al.*, 1993; Hermanns *et al.*, 1995; Eaton *et al.*, 1996; Happonen *et al.*, 1996 and Yamasaki *et al.*, 1998). Studies have thus far failed to clarify the significance of gastric Helicobacters (Happonen, 2000).

In human beings *H. pylori* has been demonstrated to play an important role in gastritis, gastroduodenal ulceration, gastric adenocarcinoma and gastric mucosa associated lymphoma (Sipponen *et al.*, 1993 and Parsonnet, 1993).

2.7.4. DIAGNOSIS

Strauss-Ayali and Simpson (1999) stated that the diagnostic tests for gastric *Helicobacter spp.* can be either invasive or noninvasive. Invasive tests like culture, histopathology, touch cytology, biopsy urease test, electron microscopy and PCR require gastric biopsies, which are usually acquired endoscopically from anesthetized dogs. Noninvasive tests like serology and urea breath and blood tests (UBBTs) do not require biopsies.

Megraud (1996) summarized the sensitivity and specificity of various diagnostic tests in the diagnosis of *H. pylori* in human patients.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (Percentage)</th>
<th>Specificity (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology</td>
<td>93.6</td>
<td>97.7</td>
</tr>
<tr>
<td>Culture</td>
<td>98.4</td>
<td>100</td>
</tr>
<tr>
<td>PCR</td>
<td>96.7</td>
<td>100</td>
</tr>
<tr>
<td>Rapid urease test</td>
<td>90.2</td>
<td>100</td>
</tr>
</tbody>
</table>
13C Urea breath test  100     100  
Serology  98.4     88.4

2.7.4.1. Invasive tests

2.7.4.1.1. Rapid urease test (rut)

_Helicobacter spp._ has a special property of liberating an enzyme called urease, which splits urea into ammonia and bicarbonate (Strauss-Ayali and Simpson, 1999). The test reagent contains urea and phenol red at pH 6.8 either in solution (locally made rapid urease test) or in gel form (commercial urease test kit). After inoculation of gastric biopsy specimen into the reagent, the bacterial urease cleaves the urea and the pH change is indicated by a color change from yellow to pink.

Sensitivity and specificity of RUT had been validated by many studies (Marshal _et al._, 1987 and Chu _et al._, 1997). However, the sensitivity of the test depends upon the number of bacteria in the biopsy. It has been calculated that $10^4$ organisms are required for a positive result (Bourguignon, 1989). Treatment with anti-_H. Pylori_ drugs or anti-secretory drugs reduce the density of bacteria and are therefore associated with decreased sensitivity of RUT (Chu _et al._, 1997).

2.7.4.1.2. Culture

Fox (1998) opined that the culture and isolation of specific _Helicobacter spp._ remains the definitive diagnosis and explained the difficulty in culturing of these organisms in artificial media. Strauss-Ayali and Simpson (1999) reported that now it is possible to culture many _Helicobacter spp._

Various authors used different agars for culturing of _Helicobacter spp._ A brucella agar base supplemented with 5 per cent sheep blood containing trimethoprim, vancomycin, and polymyxin B (Handt _et al._, 1994; 1995). Brucella agar with 10 per cent horse blood containing vancomycin (10 mg/L), polymyxin B (2500 U/L) and
trimethoprim (5 mg/L) (Fox, 1998), Blood agar containing Skirrow’s supplement (Eaton et al., 1996), blood agar with trimethoprim-vancomycin-polymyxin (Fox et al., 1996).

Brain-heart infusion (BHI) blood agar containing trimethoprim 2.5 μg/ml and cycloheximide 50 μg/ml (Happonen et al., 1998), CUA medium containing cefoperazone, vancomycin and amphotericin B and Helicobacter selective medium containing nalidixic acid, polymyxin B, amphotericin B, bacitracin and vancomycin (Fox et al., 2001). However, all authors suggested that the plates are to be incubated for at least 7-10 days at 35 – 37°C in microaerophilic condition with 10 per cent carbon dioxide, 80 per cent nitrogen and 5 per cent hydrogen.

2.7.4.1.3. Touch cytology

Helicobacter like organisms can be visualized visually using May-Grunwald-Giemsa, Gram or Diff-Quick stains by touch cytology (Strauss-Ayali and Simpson, 1999).

2.7.4.1.4. Histopathology

Histopathology depends on the visual identification of Helicobacter like organisms (CHO3) on tissue sections from the stomach. Silver stains such as Warthin Starry stain and modified Steiner stain have been generally recommended for reliable diagnosis of HLOs (Strauss-Ayali and Simpson, 1999). Happonen et al., (1996) described similar efficacy with hematoxylin and eosin stain.

Strauss-Ayali and Simpson (1999) stressed the importance of multiple biopsies due to patchy distribution of HLOs and reported that the variability of histopathological criteria and lack of standardized canine based grading system made comparison of histopathological results between studies difficult.
2.7.4.1.5. Other advanced techniques


DNA from gastric biopsies was subjected to PCR with *Helicobacter* genus-specific primers and *Helicobacter* species-specific primers. Primers are derived from either 16 S rRNA or the urease or adhesion genes (Handt *et al.*, 1994; Handt *et al.*, 1995; Fox *et al.*, 1995; Eaton *et al.*, 1996; Tireljung *et al.*, 1998; Fox *et al.*, 2001; Poutahidis *et al.*, 2001; Figueroa *et al.*, 2002).

2.7.4.2. Noninvasive tests

In recent literatures enzyme linked immunosorbent assay (ELISA), Immunoblotting, and urea breath and Blood test (UBBT) in specific diagnosis of *Helicobacter* spp. had also been reported by several authors (Patterson *et al.*, 2000; Patterson *et al.*, 2001; Kabir, 2001 and Kobayashi *et al.*, 2002).

Strauss-Ayali and Simpson (1999) opined that these non-invasive diagnostic techniques are desirable as they involve less discomfort to both patient and owner. In humans serology is used as a screening test and urea breath test to confirm eradication after treatment.

2.7.5. *Helicobacter* spp. in uremic gastropathy

In human beings *Campylobacter pylori* can colonize the duodenal mucosal surface only in the presence of gastric metaplasia (Wyatt *et al.*, 1987). Franzin *et al.*, (1982) reported a higher incidence of gastric metaplasia in patients with chronic renal failure. Taking these into consideration Shousha *et al.*, (1989) studied the duodenal
biopsy specimens from 80 patients with chronic renal failure undergoing hemodialysis. Chronic duodenitis was identified 47 (59%) of patients of whom 7 (9%) showed evidence of active inflammation. _C. pylori_ was identified in only two patients (2.5%), though gastric metaplasia was present in 50 (62.5%) patients and concluded that despite presence of gastric metaplasia, the duodenal environment remained hostile to _C. pylori_ in patients with chronic renal failure.

Shousha (1989) concluded that the prevalence of antral _Helicobacter pylori_ in patients with chronic renal failure (24%) was similar to that reported in normal healthy volunteers (11-27%). However, the prevalence was significantly less than the control group (42%).

Kao _et al._ (1995) reported the incidence of _H. pylori_ infection in hemodialysis and non hemodialysis human patients as 45% and 65% respectively.

Chhina _et al._ (1998) reported the incidence of _H. pylori_ in chronic renal failure patients as 42% and concluded that chronic renal failure patients especially those on dialysis should be tested for the presence of _H pylori_ infection as the diagnosis is of immense significance for medical management.

Polzin and Osborne (1995) opined that a possible mechanism for normal or decreased gastric acidity in uremia is neutralization of gastric acid by elevated concentrations of ammonium ions in gastric fluids due to the action of bacterial urease on gastric urea. In humans _Helicobacter pylori_ infection has been associated with increased gastric ammonia levels in uremia (Tviebling _et al._, 1999 and Kang, 1993).

Kavitha (1997) isolated _Helicobacter spp._ from antral biopsy samples obtained from uremic dogs.
CHAPTER - III

MATERIALS AND METHODS

The study was conducted at the Centre of Advanced Studies in Veterinary Clinical Medicine, Ethics and Jurisprudence, Madras Veterinary College, Chennai – 7 for a period of five semesters during the year 2001-2003.

3.1. DESIGN OF STUDY

The study consisted of apparently healthy dogs and clinical cases. Ten apparently healthy dogs from Tamil Nadu Commando School, Dog Squad were included as apparently healthy animals for comparison of various parameters under study. Clinical study was conducted with the dogs brought to small Animal Clinic, Out patient Medical Unit of Madras Veterinary College hospital.

3.1.1. Control animals

Ten apparently healthy dogs from Tamil Nadu Commando School, Dog Squad were selected as control animals for obtaining normal data including gastroduodenoscopic studies for comparison with clinical cases for the parameters under study.

3.1.2. Clinical study

The dogs with clinical signs suggestive of chronic renal failure were subjected to detailed physical examination, hematology, serum biochemistry, fecal examination, urinalysis and nephrosonography. The dogs with renal failure were then grouped as mild (SUN ≤ 50 mg/dl), moderate (SUN - 50 to 90 mg/dl), severe (SUN - 90 to 140 mg/dl), and very severe (SUN ≥ 140 mg/dl) based on the degree of azotemia (Mitch, 1991). Gastroduodenoscopy was carried out to study the gastric mucosal changes in all five groups. Endoscopy guided mucosal biopsy was done in all clinical cases.
3.2. GROUPING

3.2.1. Group I (n = 10)
   Control animals

3.2.2 Group II (n = 6)
   Mild azotemia (SUN \leq 50 \text{ mg/dl})

3.2.3. Group III (n = 8)
   Moderate azotemia (SUN = 50 to 90 \text{ mg/dl})

3.2.4. Group IV (n = 8)
   Severe azotemia (SUN = 90 to 140 \text{ mg/dl})

3.2.5. Group V (n = 13)
   Very severe azotemia (SUN \geq 140 \text{ mg/dl})

3.3. CHARACTERS UNDER STUDY

   The following parameters were studied in all five groups.

   i. History

   ii. Clinical Signs

   iii. Hemogram

   iv. Leukogram

   v. Serum biochemical profile

   vi. Fecal examination

   vii. Routine urinalysis

   viii. Nephrosonography

   ix. Gastroduodenoscopy and mucosal biopsy

   x. Histopathology and endoscopic guided gastric mucosal biopsy

   xi. Isolation of Helicobacter spp.

   xii. Post mortem examination whenever applicable
3.4. EVALUATION OF VARIOUS PARAMETERS

3.4.1. CLINICAL SIGNS

The dogs selected for the present study were subjected to a detailed clinical examination and the results were recorded in a proforma specially designed for collection of data (Appendix – I).

3.4.2. HEMATOLOGY

Blood was collected in a dry vial containing 10% ethylene diamine tetraacetate (EDTA) for red blood cell (RBC) count, white blood cell (WBC) count, hemoglobin (Hb) and packed cell volume (PCV), peripheral blood smears were made for differential counts (Jain, 1986). Erythrocyte indices were calculated as described by Coles (1986).

3.4.3. SERUM BIOCHEMICAL PROFILE

Blood was collected in a vaccutainer with no additive from either saphenous or cephalic vein for biochemical studies.

3.4.3.1. Serum urea nitrogen  (SUN)

Serum Urea Nitrogen was estimated by Diacetyl monozime method (Marsh et al., 1965)

3.4.3.2. Serum creatinine

Serum creatinine was estimated by Jaffe’s Alkaline Picrate method (Bauer et al., 1974).

3.4.3.3. Serum total protein and albumin

Serum total protein and albumin were determined by modified Biuret and Dumas method cited by Bauer et al. (1974).
3.4.3.4. **Serum electrolytes**

Serum potassium was analyzed by colorimetric method as described by Sunderman and Sunderman (1959) and serum phosphorus was estimated by modified Mesol method as described by Daly (1972).

3.4.4. **FECAL EXAMINATION**

Feces was collected from animals and subjected to occult blood test (Boddie, 1970).

3.4.5. **URINALYSIS**

Urine was collected from animals and subjected to routine urinalysis as described by Chauhan (1995).

3.4.6. **NEPHROSONOGRAPHY**

3.4.6.1. **Preparation and restraint of patient**

The hair over the entire abdomen was clipped including midway up the body wall over the right and left caudal intercostal spaces. Nephrosonographic examination was performed in either dorsal or lateral recumbency. A liberal amount of acoustic coupling gel was applied to provide sufficient contact (Nyland, *et al.*, 1995).

3.4.6.2. **Instrumentation**

Nephrosonographic studies were carried out using scanner 200(R), ultrasound scanner with 3.5 MHz, 5 MHz, and 7.5 MHz transducers. For medium to large breed dogs 3.5 MHz, and 5 MHz transducers were used. 5 MHz, and 7.5 MHz transducers were used in small dogs.

3.4.6.3. **Nephrosonographic technique**

After patient preparation, the left kidney was imaged caudal to the greater curvature of stomach caudodorsal to the spleen, lateral to the aorta and left adrenal gland at the level of the L2 to L4 vertebrae. The right kidney was imaged caudal to the
right liver lobes, lateral to the caudal vena cava and right adrenal gland at the level of the L₁ to L₃ vertebrae (Armbrust *et al.*, 2001). Standard coronal and transverse sections were obtained according to the established protocol (Barr, 1990).

**3.4.6.4. Interpretation of nephrosonograms**

Sonograms were evaluated for information on renal architecture, specifically including focal, multifocal or diffuse alterations in renal cortical, medullary, sinusal and perinephric echogenicity, compared with normal renal ultrasonographic anatomy and tissue echogenicity. In addition, cortical and medullary echogenicity were compared subjectively with the hepatic and splenic parenchymal echogenicity. The echogenicity of the identifiable lesion, as seen on the gray-scale 2-dimensional images were classified subjectively as normal, increased (hyperechoic), decreased (hypoechoic), or absent (anechoic), when compared with the normal echo pattern for the canine kidney (Walter *et al.*, 1987).

**3.4.7. GASTRODUODENOSCOPY**

Gastroduodenoscopy was carried out to study the gastric mucosal changes in all five groups of dogs.

**3.4.7.1. Preparation and restraint of the patient**

The stomach of the animals was emptied by withholding food 12 to 18 hours and water 4 hours before gastroduodenoscopic examination (Tams, 1990). The dogs were premedicated with diazepam 0.28 mg/kg b.wt. Intravenous. Anesthesia was induced and maintained with Ketamine 5.5 mg/kg b.wt. Intravenous (Hellyer, 1992) and the patients were placed in left lateral recumbency for gastroduodenoscopic procedure (Tams, 1990).
3.4.7.2. Instrumentation

Gastroduodenoscopic study in the apparently healthy dogs and clinical cases were conducted with gastrofiberscope OLYMPUS type GF*. The instrument has 100° field of view and 3-100 mm is the depth of field in the optical system. The total length is 1345 mm and working length is 1025 mm. The inner diameter of the instrument channel is 2 mm, while the outer diameter of the insertion tube is 9 mm. The bending section has the maximum deflection range of 240° and the range of tip bending up - 210°, down - 90°, right - 100° and left - 100°.

3.4.7.3. Gastroduodenoscopic procedure

Before every gastroduodenoscopic procedure the instrument was sterilized with 2% glutaraldehyde, washed with distilled water and dried by aspirating air. Then the working condition of the gastrofiberscope was checked. The head of patient was held by a assistant and the mouth gag was tightly secured and rechecked. The control unit was held in left hand and the insertion section was introduced through the mouth gag into oral cavity, pharynx and esophagus. After entering esophagus the instrument is advanced caudally with intermittent air insufflation. After reaching the caudal esophagus the position and configuration of gastroesophageal junction was noted. The endoscope tip is then advanced through the gastroesophageal junction by deflecting the tip slightly to the left and simultaneous slight upward deflection. After entering the stomach an overview and orientation within the gastric lumen was obtained. Air insufflation was done until the rugal folds begin to separate. The tip is gradually advanced through the proximal stomach along the greater curvature and once the angulus and antrum are reached the tip was directed through the pyloric canal to duodenum. After duodenoscopy pylorus was examined thoroughly. Finally a
retroversion maneuver was performed and the angulus, cardia and fundus were examined thoroughly (Tams, 1990).

3.4.7.4. **Gastroscopy aided mucosal biopsy**

The biopsy forceps was passed through the biopsy channel of the endoscope and guided precisely to the biopsy site. Biopsy of gastric antral mucosa was taken from the margin of the lesion. Random biopsies of pyloric antrum were taken in the absence of lesions (Tams, 1990). Four biopsy specimen were obtained for routine histopathology, special staining for identifying *Helicobacter spp.*, rapid urease testing and culture of *Helicobacter spp.* respectively.

3.4.8. **HISTOPATHOLOGICAL EXAMINATION OF BIOPSY SAMPLES**

Gastric biopsy specimen for histopathologic evaluation was fixed in neutral buffered formalin (10%) solution immediately after collection. The specimen were embedded in paraffin, cut into the thickness of 3 to 4 µm and stained with Haematoxylin and Eosin method as described by Luna (1968). Histopathological changes in the gastric mucosa were recorded.

3.4.9. **ISOLATION OF HELICOBACTER SPP.**

3.4.9.1. Rapid urease test

The urease test was performed on specimen obtained from all dogs. To perform the rapid urease test, a mucosal biopsy specimen was placed into a test reagent containing 10% unbuffered urea in distilled water and 1% phenol red, the specimen were then incubated at room temperature and the time taken for a positive result (i.e. change from light yellow to bright pink) was recorded (Happonen *et al.*, 1998).
3.4.9.2. Culture and isolation of *Helicobacter* spp.

The biopsy specimen were submitted to bacterial culture within 2 to 8 hours after endoscopy. Specimen were transported in a special transport medium (Brain – heart infusion broth) with ice. The specimen were swabbed on Brucella agar enriched with brucella selective supplement and 10% horse blood containing selected antibiotics (trimethoprim 2.5 mg/ml; vancomycin 5 µg/ml and polymixin – B 1.25 µg/ml). Plates were then incubated at 37°C, microaerobically with 5% O₂, 10% CO₂ and 85% N₂ for 10 days. Growth was usually visible as thin film 3 to 10 days after start of incubation. Preliminary identification of *Helicobacter* spp. was made by morphological characteristics of Gram and Giemsa stained smears.

3.4.9.3. Histopathological examination of gastric biopsy

Gastric biopsy specimen for identification of *Helicobacter* spp. were fixed in 10% neutral buffered formalin, embedded in paraffin, cut into the thickness of 3-4 µm and stained with Toluidine blue in Sorenson’s phosphate buffer as described by Stevens and Francis (1996).

3.5. CLEANING AND STORAGE OF GASTROFIBERSCOPE

After the endoscopic procedure the gastroscope was cleaned sterilized and placed in the endoscopy rack as per the procedure suggested by (Tams, 1990).

3.6. STATISTICAL ANALYSIS

The data collected were subjected to statistical analysis as per Snedecor and Cochran (1994) and critically discussed.
CHAPTER – IV

RESULTS

The dogs presented at the Small Animal Clinic of the Madras Veterinary College Hospital campus were screened for renal failure. Out of these, 35 dogs found to be suffering from renal failure were selected for the present study. Based on Blood Urea Nitrogen (BUN) values these animals were classified as mild (Group II, n=6), moderate (Group III, n=8), severe (Group IV, n=8) and very severe (Group V, n=13) stage of renal failure.

Ten dogs from the Tamil Nadu Commando School, dog squad were included as apparently healthy animals (Group I, n=10) for comparison of various parameters under study.

A detailed clinical, hematological, serum biochemical, urinalysis, fecal occult blood test, endoscopy, endoscopy guided mucosal biopsy studies were carried out in all the five groups.

4.1. INCIDENCE

4.1.1. Age

The age wise incidences of renal failure in dogs in the present study are given in Fig.2.

Out of thirty-five dogs with renal failure, eight were below five years (22.86%), twelve were between five to ten years (34.29%) and fifteen were above ten years (42.85%).

4.1.2. Breed

The incidences of renal failure in different breeds of dogs selected for this study are given in Fig.3.
AGE WISE INCIDENCE OF RENAL FAILURE IN DOGS

- 43% < 5 years
- 23% 5-10 years
- 34% > 10 years
Fig – 3

INCIDENCE OF RENAL FAILURE IN DIFFERENT BREEDS

Labrador: 26%
GSD: 20%
ND: 17%
Spitz: 17%
Lhas: 11%
Dane: 6%
Rajapalayam: 3%
SEX WISE INCIDENCE OF RENAL FAILURE

- Male: 54%
- Female: 46%
Out of thirty-five dogs with renal failure, the breed wise incidences were, nine – Labrador retrievers (25.72%), seven - German Shepherds (20.00%), six – Non descripts (17.14 %), six – Spitz (17.14%), four – Lhasa apsos (11.43%), two – Great Danes (5.71%) and one – Rajapalayam (2.86%).

4.1.3. Sex

The sex wise incidences of renal failure in dogs selected for this study are given in Fig.4.

Out of thirty-five dogs selected for the present study nineteen (54.29%) were male and sixteen (45.71%) were female dogs.

4.2. GASTROINTESTINAL SIGNS NOTICED IN CANINE RENAL FAILURE

The gastrointestinal signs noticed in the thirty-five dogs selected for the present study are given in Fig. 1.

The gastrointestinal signs include anorexia in 29 dogs (82.86%), vomiting in 26 dogs (74.29%) out of which ten dogs (38.46%) had yellowish vomitus, six dogs (23.08%) had whitish vomitus, eight dogs (30.77%) had brownish vomitus and two dogs (7.69%) had hematemesis, halitosis in 18 dogs (51.43%), and oral ulcers (Plates-1,2,3) in twelve dogs (34.29%).

Abnormal consistency of motion was noticed in twenty five dogs (71.43%) out of which thirteen dogs (52.00%) had watery motion and twelve dogs (48.00%) had semisolid motion. Abnormal colour of motion was noticed in twenty dogs (57.14%) out of which twelve dogs (60.00%) had brownish stools and eight dogs (40.00%) had blackish stools.

In the present study dehydration was noticed in thirty dogs (85.71%) out of which eight dogs (26.67%) had dehydration between six to eight per cent, twelve dogs (40.00%) had dehydration between eight to ten percent, eight dogs (26.67%) had
GASTROINTESTINAL SIGNS NOTICED IN CANINE RENAL FAILURE

- Dehydration
- Abnormal motion colour
- Abnormal motion consistency
- Oral ulcers
- Halitosis
- Vomiting
- Anorexia

Yellowish
Whitish
Brownish
Hematemes
Watery
Semisolid
Browish
Blackish
6%-8%
8%-10%
10%-12%
>12%

PERCENTAGE
Plate - 1: Tongue ulcer

Plate - 2: Tongue ulcer (Endoscopical view)

Plate - 3: Tongue ulcer (Endoscopical view)
dehydration between ten to twelve per cent and two dogs (6.66%) had dehydration above twelve per cent.

4.3. ERYTHRON

The mean ± S.E. values and F – ratio for erythron of group I, group II, group III, group IV and group V are given in table 1.

The mean ± S.E. values of hemoglobin recorded in the five groups were 14.10 ± 0.34 g/dl, 10.25 ± 1.81 g/dl, 12.19 ± 0.93 g/dl, 9.35 ± 1.29 g/dl and 7.10 ± 0.65 g/dl respectively. A highly significant decrease in hemoglobin values were observed in group II, group IV, and group V when compared to the control group. A non-significant decrease in group III was observed when compared to control group.

The mean ± S.E values of packed cell volume recorded in the five groups were 44.00 ± 1.33 per cent, 38.17 ± 6.78 per cent, 40.63 ± 2.29 per cent, 31.00 ± 4.33 per cent and 25.39 ± 2.15 per cent respectively. A highly significant decrease in packed cell volume was observed in group IV and group V when compared to control group and a non significant decrease in packed cell volume was observed in group II and group III when compared to control group.

The mean ± S.E. values of red blood cell count observed in all five groups were 6.13 ± 0.16 million/cu.mm, 5.64 ± 0.99 million/cu.mm, 5.86 ± 0.33 million/cu.mm, 4.84 ± 0.60 million/cu.mm and 4.29 ± 0.32 million/cu.mm respectively. A significant decrease in red blood cell count was observed in group V when compared to control group and a non significant decrease in group II, group III and group IV was observed when compared to control group.

4.4. ERYTHROCYTE INDICES

The mean ± S.E. values and F – ratio of MCV, MCH and MCHC in all five groups are given in Table 2.
The mean ± S.E. values of MCV recorded in all five groups were 68.09 ± 1.66 fl, 68.42 ± 2.73 fl, 69.71 ± 2.36 fl, 63.41 ± 2.96 fl and 60.97 ± 2.66 fl respectively. The mean ± S.E. values of MCH recorded in all five groups were 21.98 ± 0.97 pg, 18.60 ± 1.21 pg, 20.85 ± 1.17 pg, 21.26 ± 2.42 pg and 17.38 ± 0.98 pg respectively. The mean ± S.E. values of MCHC recorded in all five groups were 33.44 ± 0.98 per cent, 32.57 ± 0.22 per cent, 31.94 ± 0.66 per cent, 31.58 ± 0.19 per cent and 31.42 ± 0.31 per cent respectively.

There was no significant difference in the erythrocyte indices of all five groups.

4.5. LEUKOGRAM

The mean ± S.E. values and F – ratio of Leukogram in all five groups are given in Table- 3.

The mean ± S.E. values of white blood cell count in all five groups were 8160.00 ± 384.77 /cu.mm, 16083.33 ± 8012.67 /cu.mm, 22562.50 ± 8428.48 /cu.mm, 17875.00 ± 2953.86 /cu.mm and 23969.23 ± 4084.92 /cu.mm respectively. Though no significant difference in white blood cell count was observed between all five groups, a non significant increase in white blood cell count was observed in group II, group III, group IV and group V when compared to control group.

The mean ± S.E. values of neutrophils in all five groups were 5787.00 ± 327.35 /cu.mm, 7384.67 ± 1978.30 /cu.mm, 18325.00 ± 7472.59 /cu.mm, 14111.38 ± 2804.00 /cu.mm and 20043.69 ± 3606.65 /cu.mm respectively. No significant difference was observed in group II and group IV where as significant increase in neutrophil count was observed in group III and group V when compared to the control group.
The mean ± S. E. values of lymphocytes in all five groups were 2196.40 ± 123.95 /cu.mm, 7954.00 ± 5578.57 /cu.mm, 3656.75 ± 725.83 /cu.mm, 3240.88 ± 507.50 /cu.mm and 3207.23 ± 894.50 /cu.mm respectively. No significant difference in lymphocyte count was observed between all five groups.

The mean ± S.E. values of monocytes in all five groups were 149.10 ± 41.75 /cu.mm, 705.33 ± 537.27 /cu.mm, 239.50 ± 91.64 /cu.mm, 207.25 ± 113.87 /cu.mm and 486.62 ± 136.60 /cu.mm respectively. No significant difference in monocyte count was observed between all five groups.

The mean ± S.E. values of eosinophils in all five groups were 27.50 ± 21.28 /cu.mm, 39.33 ± 26.74 /cu.mm, 416.25 ± 330.01 /cu.mm, 315.50 ± 183.07 /cu.mm and 230.92 ± 101.68 /cu.mm respectively. No significant difference in eosinophil count was observed between all five groups.

4.6. SERUM BIOCHEMICAL PROFILE

The mean ± S.E. values and F – ratio of serum biochemical profile are given in Table 4.

4.6.1. Serum urea nitrogen (SUN)

The mean ± S.E. values of serum urea nitrogen in all five groups were 12.00 ± 1.19 mg/dl, 28.33 ± 4.77 mg/dl, 75.90 ± 4.45 mg/dl, 122.00 ± 4.06 mg/dl and 265.55 ± 30.52 mg/dl respectively. A non significant increase in serum urea nitrogen values was observed in group II and group III when compared to control group. A highly significant increase in serum urea nitrogen values were observed in group IV and group V when compared to control group.
4.6.2. Serum creatinine

The mean ± S.E. values of serum creatinine in all five groups were 0.83 ± 1.13 mg/dl, 3.30 ± 0.87 mg/dl, 3.25 ± 0.28 mg/dl, 5.54 ± 1.33 mg/dl and 7.60 ± 1.07 mg/dl respectively. A highly significant increase in serum creatinine values was observed in group IV and group V when compared to the control group. No significant differences in serum creatinine values were observed in group II and group III when compared to control group.

4.6.3. Total protein, albumin and globulin

The mean ± S.E. values of total protein in all five groups were 7.08 ± 0.19 g/dl, 7.05 ± 0.25 g/dl, 6.70 ± 0.17 g/dl, 5.31 ± 0.79 g/dl and 6.08 ± 0.33 g/dl respectively. The mean ± S.E. albumin values in all five groups were 4.08 ± 0.16 g/dl, 3.67 ± 0.14 g/dl, 3.05 ± 0.24 g/dl, 2.51 ± 0.40 g/dl and 2.07 ± 0.14 g/dl respectively. The mean ± S.E. values of globulin values in all five groups were 3.00 ± 0.08 g/dl, 3.37 ± 0.30 g/dl, 3.65 ± 0.14 g/dl, 2.80 ± 0.53 g/dl and 3.05 ± 0.30 g/dl respectively.

No significant differences in total protein values were observed in group II and group III when compared to the control group. A significant decrease in total protein values was observed in group IV and group V when compared with the control group.

No significant difference in serum albumin values were observed in group II and highly significant decrease in serum albumin values were observed in group III, group IV and group V when compared with the control group.

No significant difference in serum globulin values were observed in group II, group III, group IV and group V when compared to the control group. A significant increase in serum globulin values of group V was observed when compared to the control group.
4.6.4. Serum potassium

The mean ± S.E. values of serum potassium values in all five groups are 4.18 ± 0.34 mEq/L, 4.52 ± 0.18 mEq/L, 4.33 ± 0.21 mEq/L, 3.97 ± 0.45 mEq/L and 4.41 ± 0.37 mEq/L respectively. No significant differences in serum potassium values were observed between all five groups.

4.6.5. Serum phosphorus

The mean ± S.E. values of serum phosphorus values in all five groups are 4.71 ± 0.31 mg/dl, 4.55 ± 0.21 mg/dl, 4.56 ± 0.20 mg/dl, 4.33 ± 0.68 mg/dl and 5.39 ± 0.57 mg/dl respectively. No significant differences in serum phosphorus values were observed between all five groups.

4.7. URINALYSIS

A moderate proteinuria (+++) with epithelial cell casts was observed in four animals of group IV.

A severe proteinuria (++++) with epithelial cell casts was observed in four animals and severe proteinuria (++++) with pus cells was observed in three animals in group V. The urinalysis of group II, group III showed no detectable abnormalities.

4.8. FECAL OCCULT BLOOD TEST

A positive occult blood result was noticed in one dog from group II and group III three dogs from group IV and six dogs from group V respectively.

4.9. NEPHROSONOGRAPHY

The nephrosonographic findings in control and clinical cases are summarized in Table 5.

In control group the sonographic architecture presented a complex picture containing a mixture of hyperechoic, hypoechoic and anechoic patterns. In comparison, most of other organs in the abdomen revealed a more homogenous
Plate - 4: Nephrosonogram - Left Kidney
Corticomedullary distinction not clear

Plate - 5: Nephrosonogram - Right Kidney
Corticomedullary distinction not clear
Plate - 6: Nephrosonogram - Left Kidney
Corticomедullary distinction absent

Plate - 7: Nephrosonogram - Right Kidney
Corticomедullary distinction absent
Plate - 8: Nephrosonogram - Left Kidney
Hyperechoic cortex

Plate - 9: Nephrosonogram - Right Kidney
Hyperechoic cortex
Plate - 8: Nephrosonogram - Left Kidney
Hyperechoic cortex

Plate - 9: Nephrosonogram - Right Kidney
Hyperechoic cortex
Plate - 10: Nephrosonogram - Left Kidney
Hyperechoic medullary rim

Plate - 11: Nephrosonogram - Right Kidney
Hyperechoic medullary rim
picture. The major regions of the kidney included the echogenic cortex, the less echogenic medulla, and the hyperechoic renal pelvis. The areas of the kidney could be ranked in decreasing order of echogenicity as follows, 1. Capsule, 2. Diverticula and vasculature, 3. Renal sinus, 4. Cortex and 5. Medulla.

Out of six animals in group II, corticomedullary distinction was not clear (Plates –4,5) in three cases and a normal nephrosonogram was observed in the remaining three cases.

Out of eight animals in group III, corticomedullary distinction was not clear (Plates-4,5) in five cases, hyperechoic cortex (Plates-8,9) in one case and hyperechoic medullary rim sign (Plates-10,11) in two cases.

In group IV out of eight animals, corticomedullary distinction was not clear (Plates-4,5) in three cases, corticomedullary distinction was absent (Plates-6,7) in one case, hyperechoic cortex (Plates-8,9) in two cases, medullary band sign in one case and normal nephrosonogram in one case.

Out of thirteen animals in group V, corticomedullary distinction was not clear (Plates-4,5) in six cases, corticomedullary distinction absent (Plates-6,7) in four cases, hyperechoic cortex (Plates-8,9) in two cases and hyperechoic medullary rim sign (Plates-10,11) in one case.

4.10. ENDOSCOPY

4.10.1 Gastroduodenoscopy

The gastroduodenoscopic findings in control and clinical cases are summarized in Table 6.
Plate - 12: Endoscopy
- Normal Oesophagus

Plate - 13: Endoscopy
- Hyperemic Oesophagus

Plate - 14: Endoscopy
- Oesophageal erosions

Plate - 15: Endoscopy
- Normal LES
Plate - 24: Endoscopy
Antral biopsy

Plate - 25: Endoscopy
Normal duodenum

Plate - 26: Endoscopy
Duodenal ulcers
4.10.1.1. Esophagus

In the control group the esophagus was found collapsed and upon insufflation the mucosa was pale pink with fine submucosal vessels (Plate-12). The lower esophageal sphincter was closed and had a irregular rosette appearance (Plate-15).

In group II one case had a pale esophageal mucosa with erosions in caudal esophagus. Similarly pale pink mucosa with hyperemia and erosions in the esophagus (Plate-13) was observed in two cases in group III and group IV respectively. In group V pale esophageal mucosa, mucosal irregularity and erosions (Plate-14) was noticed in six cases.

4.10.1.2. Lower esophageal sphincter (LES)

In control group the lower esophageal sphincter was closed and had a irregular rosette appearance (Plate-15). One animal in group II and two animals in group III showed hyperemic changes in LES. Two animals in group IV and six animals in group V showed hyperemic changes and erosions (gastric reflux?) in LES (Plate-16).

4.10.1.3. Cardia

The cardia of the stomach was uniformly dark pink and no lesions were found in cardia of animals in all five groups.

4.10.1.4. Fundus

In control group after entering into fundus the mucosa was dark pink, rugal folds were noticed on the greater curvature. On insufflation the rugal folds began to separate.

Two animals in group III, two animals in group IV and six animals in group V showed hyperemic changes and linear erosions in the fundus (Plates-17,18,19).
4.10.1.5. Antrum and pylorus

In control animals there were no rugal folds and peristaltic contractions (Plate-20) observed in the antrum.

In group II one animal showed linear erosions (Plate-22) in pyloric antrum. In group III two animals had bile in the antrum. Two animals in group IV and six animals in group V had erosions and bleeding ulcers in the pyloric antrum (Plates-21,23).

4.10.1.6. Duodenum

In control animals the duodenum was pink, smooth and uniform (Plate-25). In group II one animal showed erosions in duodenal mucosa (Plate-26). Two animals in group IV and six animals in group V had erosions and ulcers (Plate-26) in duodenum.

4.10.2 Histopathology of endoscopy guided mucosal biopsy

Endoscopy guided mucosal biopsy was done on the lesion sites (Plate-24) in animals with lesions and random biopsies of pyloric antrum in animals without lesions were taken. Histopathological examination of these biopsies were done.

In group II three animals showed mild fibrosis of lamina propria (Plate-28), mild submucosal fibrosis and distension of gastric glands (Plate-27), one dog showed submucosal fibrosis and hemorrhage (Plate-29).

In group III two animals had submucosal fibrosis, atrophy of gastric glands with mononuclear cell infiltration (Plate-30), one animal showed submucosal fibrosis with increased goblet cell activity (Plate-31).

In group IV two dogs had increased goblet cell activity, submucosal hemorrhage (Plate-32) one dog had submucosal fibrosis and one dog had mucosal hyperplasia (Plate-33).
Plate - 27: Gastric biopsy - Submucosal fibrosis and distension of gastric glands (H & E x 320)

Plate - 28: Gastric biopsy - Fibrosis of Lamina propria (H & E x 320)

Plate - 29: Gastric biopsy - Submucosal haemorrhage and fibrosis (H & E x 320)
Plate - 30: Gastric biopsy - Submucosal fibrosis atrophy of gastric glands with mononuclear cell infiltration (H & E x 320)

Plate - 31: Gastric biopsy - Increased goblet cell activity (H & E x 320)

Plate - 32: Gastric biopsy - Submucosal fibrosis and increased goblet cell activity (H & E x 320)
Plate - 33: Gastric biopsy - Hyperplastic changes (H & E x 125)

Plate - 34: Gastric biopsy - Severe fibrosis and ulceration (H & E x 320)

Plate - 35: Gastric biopsy - Atrophy of Gastric glands, fibrosis and ulceration (H & E x 320)
In group V six dogs revealed severe fibrosis and ulceration (Plate-34), two dogs with more severe fibrosis and ulceration (Plate-35), three dogs showed hyperplastic changes (Plate-33), one dog showed atrophy of gastric glands (Plate-35), one dog had ulceration, submucosal congestion and fibrosis and one dog had glandular hyperplasia with mononuclear cell infiltration.

4.11. Isolation of helicobacter spp.

During gastroduodenoscopic examination three biopsy specimen were collected and subjected to rapid urease testing, culture of Helicobacter spp. and histopathological examination respectively. The results of rapid urease testing, culture and histopathology in the isolation of Helicobacter spp. are summarized in Table 7.

4.11.1. Rapid urease test (RUT)

Rapid urease testing was done in all control and clinical cases. To perform the rapid urease test, a mucosal biopsy specimen was placed into the yellow coloured test reagent containing 10 per cent unbuffered urea in distilled water and 1 per cent phenol red. The specimen were then incubated at room temperature. A change from yellow to red/dark pink in rapid urease test within 12 hours of placing the biopsy in the medium was regarded as indicative of the presence of Helicobacter spp. (Plate-36).

Three dogs in control group, one dog in group II, four dogs in group III, three dogs in group IV and eight dogs in group V had a colour change with in 12 hours of incubation at room temperature.

4.11.2. Culture of helicobacter spp

Culturing of gastric antral biopsy specimens were done in all control and clinical cases regardless of the presence of endoscopic lesions. Culture of gastric tissues from one dog in group IV and three dogs from group V had pin point, clear,
translucent colonies on Brucella agar enriched with Brucella selective supplement and 10 per cent horse blood containing selected antibiotics. Although colonies could occasionally be seen on the culture plates by three days post inoculation, usually 5 to 7 days incubation was necessary to visualize the colonies. These colonies were later found to be urease positive.

The organisms obtained in cultures of one dog form group IV and three dogs from group V were identified as *Helicobacter* spp. on the basis of their appearance as gram negative, curved rods on Gram staining (Plate-38), Giemsa staining (Plate-37) and urease production (Plate-39) in biochemical testing.

Out of three dogs in group V which had a positive culture, Helicobacter spp could not be identified in histopathology in one dog.

4.11.3. Histopathologic findings

4.11.3.1. Detection of *helicobacter* spp.

*Helicobacter* spp. were identified in one dog in group IV and three dogs in group V (Plate-40). The bacteria were practically unidentifiable by H & E staining. The toluidine blue stain in Sorenson’s phosphate buffer was more effective for detecting *Helicobacter* spp. (Plate-40). The bacteria were easily identifiable in gastric mucosa sections by virtue of their characteristic morphology and positioning. Bacteria were S – shaped or curved, but some straightened forms were also observed. *Helicobacter* spp. were located in gastric mucous and were closely associated with the surface of the gastric epithelium.

With light microscopy it was not possible to determine the nature of this close association. No bacterial cells could be identified after thorough examination of gastric mucosal biopsies of the remaining animals in all five groups, stained with Toluidine blue stain in Sorenson’s phosphate buffer and H & E.
Plate - 36: Rapid Urease Test

Plate - 37: Helicobacter Spp. (Giemsa x 1000)

Plate - 38: Helicobacter Spp. (Gram's x 1000)
Plate - 39: Biochemical testing

Plate - 40: Gastric Biopsy - Helicobacter Spp. adherent to the Gastric epithelium. (Toluidine blue in Sorenson's phosphate buffer x 1000)
4.11.3.2. Histopathologic changes

The histopathologic changes in the gastric mucosal biopsies that had *Helicobacter* spp. were also studied after staining with H & E. The dog with *Helicobacter* associated gastritis in group IV had increased goblet cell activity and submucosal hemorrhage (Plate-32). Among the three dogs with *Helicobacter* associated gastritis in group V, one dog had severe fibrosis and ulceration (Plate-34), one dog had chronic gastritis with atrophy of gastric glands (Plate-35) and one dog had glandular hyperplasia with mononuclear cell infiltration.

Among the three dogs in group V which had *Helicobacter* associated gastritis, *Helicobacter* spp failed to grow in culture in one dog.

Out of 35 clinical cases one dog in group IV and two dogs in group V had positive results in both culture and histopathology. In group V, one dog showed positive result in culture but *Helicobacter* spp. was not identified in histopathology and one dog has positive result in histopathology but *Helicobacter* spp. failed to grow in culture.

4.12. POSTMORTEM FINDINGS

Post mortem examination was conducted in fifteen animals, which died despite medical management. One dog from group II, three dogs from group III, four dogs from group IV and seven dogs from group V died despite medical management.

4.12.1. Gross pathology

A moderate to severe adhesion of the capsule to the cortical surface, pitting and granularity of the cortex were noticed in majority of cases (Plate-41). Irregular cortical surface, a few pale foci of the cortex and congestion of the cortico-medullary junction were also recorded (Plate-42).
4.12.2 Histopathology

In group II kidney showed interstitial fibrosis, tubular epithelial necrosis, atrophy of isolated glomeruli and infiltration of lymphocytes indicating chronic nephritis (Plate-43) and stomach showed congestion of lamina propria.

Kidneys of two cases in group III showed homogenous eosinophilic contents in the tubular lumen (Plate-44), atrophic changes of tubular epithelium and plasma cell infiltration (Plate-45).

In group IV kidneys showed calcification of necrotic tubular epithelium (Plate-46), calcification of portion of glomeruli was also evident in two cases (Plate-47), stomach showed hyperplastic reaction indicating chronic gastritis (Plate-50).

In group V kidneys showed necrosis of renal substance indicating suppurative nephritis (Plate-48), the infiltration included lymphocytes and plasma cells in the interstitium (Plate-49), one of the cases showed neutrophilic infiltration, necrosis of gastric epithelium.
Plate - 41: Kidneys - Irregular cortical surface with pale foci.

Plate - 42: Kidneys - Congestion of Corticomedullary junction

Plate - 43: Chronic nephritis (H & E x 125)
Plate - 44: Kidney - Tubular stasis (H & E x 320)

Plate - 45: Chronic Nephritis - Plasma cell infiltration (H & E x 320)

Plate - 46: Chronic Nephritis - Tubular calcification (H & E x 320)
Plate - 50: Stomach - Hyperplastic changes
(H & E x 125)

Plate - 51: Stomach - Epithelial necrosis
(H & E x 320)
## TABLE – 1

**COMPARISON OF ERYTHRON VALUES IN CONTROL AND CLINICAL CASES**

<table>
<thead>
<tr>
<th>S.no.</th>
<th>Parameters</th>
<th>Group-I (n=10)</th>
<th>Group-II (n=6) BUN (\leq 50) mg/dl</th>
<th>Group-III (n=8) BUN 50-90 mg/dl</th>
<th>Group-IV (n=8) BUN 90-140 mg/dl</th>
<th>Group-V (n=13) BUN (\geq 140) mg/dl</th>
<th>F-Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hb (g/dl)</td>
<td>14.10±0.34</td>
<td>10.25±1.81</td>
<td>12.19±0.93</td>
<td>9.35±1.29</td>
<td>7.10±0.65</td>
<td>9.91**</td>
</tr>
<tr>
<td>2</td>
<td>PCV(%)</td>
<td>44.00±1.33</td>
<td>38.17±6.78</td>
<td>40.63±2.29</td>
<td>31.00±4.33</td>
<td>25.39±2.15</td>
<td>6.81**</td>
</tr>
<tr>
<td>3</td>
<td>RBC (10(^6)/cu.mm)</td>
<td>6.13±0.16</td>
<td>5.64±0.99</td>
<td>5.86±0.33</td>
<td>4.84±0.60</td>
<td>4.29±0.32</td>
<td>3.34*</td>
</tr>
</tbody>
</table>

Mean ± S.E values are given in the table
Mean showing the same superscript in the rows do not differ significantly \(P > 0.05\).
F –ratio

NS- Not Significant \((P> 0.05)\)
* - Significant \((P< 0.05)\)
** - Highly Significant \((P<0.01)\)
TABLE – 2
COMPARISON OF ERYTHROCYTIC INDICES VALUES IN CONTROL AND CLINICAL CASES

<table>
<thead>
<tr>
<th>S.no.</th>
<th>Parameters</th>
<th>Group-I Control (n=10)</th>
<th>Group- II BUN≤50mg/dl (n=6)</th>
<th>Group-III BUN 50-90 mg/dl (n=8)</th>
<th>Group-IV BUN 90-140 mg/dl (n=8)</th>
<th>Group-V BUN≥ 140 mg/dl (n=13)</th>
<th>F-Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MCV (fl)</td>
<td>68.07 ± 1.66</td>
<td>68.42 ±2.73</td>
<td>69.71 ± 2.36</td>
<td>63.41 ± 2.96</td>
<td>60.97 ± 2.66</td>
<td>2.37 NS</td>
</tr>
<tr>
<td>2</td>
<td>MCH (pg)</td>
<td>21.98 ± 0.97</td>
<td>18.60 ± 1.21</td>
<td>20.85 ± 1.17</td>
<td>21.26 ± 2.42</td>
<td>17.38 ± 0.98</td>
<td>2.32 NS</td>
</tr>
<tr>
<td>3</td>
<td>MCHC(%)</td>
<td>33.44 ± 0.98</td>
<td>32.57 ± 0.22</td>
<td>31.94 ± 0.66</td>
<td>31.58 ± 0.19</td>
<td>31.42 ± 0.31</td>
<td>2.16 NS</td>
</tr>
</tbody>
</table>

Mean ± S.E values are given in the table
Mean showing the same superscript in the rows do not differ significantly P > 0.05.
F –ratio
NS- Not Significant (P> 0.05)
* - Significant (P< 0.05)
** - Highly Significant (P<0.01)
<table>
<thead>
<tr>
<th>S.no.</th>
<th>Parameters</th>
<th>Group-I Control (n=10)</th>
<th>Group-II BUN≤50mg/dl (n=6)</th>
<th>Group-III BUN 50-90 mg/dl (n=8)</th>
<th>Group-IV BUN 90-140 mg/dl (n=8)</th>
<th>Group-V BUN≥140 mg/dl (n=13)</th>
<th>F-Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>WBC (/cu.mm)</td>
<td>8160.00 ± 384.77</td>
<td>16083.33 ± 8012.67</td>
<td>22562.50 ± 8428.48</td>
<td>17875.00 ± 2953.86</td>
<td>23969.23 ± 4084.92</td>
<td>1.80 NS</td>
</tr>
<tr>
<td>2</td>
<td>Neutrophils (/cu.mm)</td>
<td>5787.00 ± 327.35</td>
<td>7384.67 ± 1978.30</td>
<td>18325.00 ± 7472.59</td>
<td>14111.38 ± 2804.00</td>
<td>20043.69 ± 3606.65</td>
<td>2.73 *</td>
</tr>
<tr>
<td>3</td>
<td>Lymphocytes (/cu.mm)</td>
<td>2196.40 ± 123.95</td>
<td>7954.00 ± 5578.57</td>
<td>3656.75 ± 725.83</td>
<td>3240.88 ± 507.50</td>
<td>3207.23 ± 844.50</td>
<td>1.25 NS</td>
</tr>
<tr>
<td>4</td>
<td>Monocytes (/cu.mm)</td>
<td>149.10 ± 41.75</td>
<td>705.33 ± 537.27</td>
<td>239.50 ± 91.64</td>
<td>207.25 ± 113.87</td>
<td>486.62 ± 136.60</td>
<td>1.29 NS</td>
</tr>
<tr>
<td>5</td>
<td>Eosinophils (/cu.mm)</td>
<td>27.50 ± 21.28</td>
<td>39.33 ± 26.74</td>
<td>416.25 ± 330.01</td>
<td>315.50 ± 183.07</td>
<td>230.92 ± 101.68</td>
<td>0.98 NS</td>
</tr>
</tbody>
</table>

Mean ± S.E values are given in the table
Mean showing the same superscript in the rows do not differ significantly P > 0.05.
F –ratio

NS- Not Significant (P> 0.05)
* - Significant (P< 0.05)
** - Highly Significant (P<0.01)
### Table 4

**Comparison of Serum Biochemical Profile in Control and Clinical Cases**

<table>
<thead>
<tr>
<th>S.no.</th>
<th>Parameters</th>
<th>Group-I Control (n=10)</th>
<th>Group-II BUN≤50 mg/dl (n=6)</th>
<th>Group-III BUN 50-90 mg/dl (n=8)</th>
<th>Group-IV BUN 90-140 mg/dl (n=8)</th>
<th>Group-V BUN≥ 140 mg/dl (n=13)</th>
<th>F-Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SUN (mg/dl)</td>
<td>12.00 ± 1.19</td>
<td>28.33 ± 4.77</td>
<td>75.90 ± 4.45</td>
<td>122.00 ± 4.06</td>
<td>265.55 ± 30.52</td>
<td>30.90 **</td>
</tr>
<tr>
<td>2</td>
<td>Creatinine (mg/dl)</td>
<td>0.83 ± 1.13</td>
<td>3.30 ± 0.87</td>
<td>3.25 ± 0.38</td>
<td>5.54 ± 1.33</td>
<td>7.60 ± 1.07</td>
<td>9.41 **</td>
</tr>
<tr>
<td>3</td>
<td>Total Protein (g/dl)</td>
<td>7.08 ± 0.19</td>
<td>7.05 ± 0.25</td>
<td>6.70 ± 0.17</td>
<td>5.31 ± 0.79</td>
<td>6.08 ± 0.33</td>
<td>3.37 *</td>
</tr>
<tr>
<td>4</td>
<td>Albumin (g/dl)</td>
<td>4.08 ± 0.16</td>
<td>3.67 ± 0.14</td>
<td>3.05 ± 0.24</td>
<td>2.51 ± 0.40</td>
<td>2.07 ± 0.14</td>
<td>16.69 **</td>
</tr>
<tr>
<td>5</td>
<td>Globulin (g/dl)</td>
<td>3.00 ± 0.08</td>
<td>3.37 ± 0.30</td>
<td>3.65 ± 0.14</td>
<td>2.80 ± 0.53</td>
<td>3.05 ± 0.30</td>
<td>3.23 *</td>
</tr>
<tr>
<td>6</td>
<td>Potassium (mEq/L)</td>
<td>4.18 ± 0.34</td>
<td>4.52 ± 0.18</td>
<td>4.33 ± 0.21</td>
<td>3.97 ± 0.45</td>
<td>4.41 ± 0.37</td>
<td>0.36 NS</td>
</tr>
<tr>
<td>7</td>
<td>Phosphorus (mg/dl)</td>
<td>4.71 ± 0.31</td>
<td>4.55 ± 0.21</td>
<td>4.56 ± 0.20</td>
<td>4.33 ± 0.68</td>
<td>5.39 ± 0.57</td>
<td>0.77 NS</td>
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</tbody>
</table>

Mean ± S.E values are given in the table.
Mean showing the same superscript in the rows do not differ significantly $P > 0.05$.
F –ratio
NS- Not Significant ($P > 0.05$)
* - Significant ($P < 0.05$)
** - Highly Significant ($P < 0.01$)
<table>
<thead>
<tr>
<th>GROUPS</th>
<th>C/M Distinction not clear</th>
<th>C/M Distinction Absent</th>
<th>Hyperechoic Cortex</th>
<th>Hyperechoic Medullary rim sign</th>
<th>Medullary Band</th>
<th>NAD</th>
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<tbody>
<tr>
<td>I</td>
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<td>---</td>
<td>---</td>
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</tr>
<tr>
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<tr>
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<td>---</td>
<td>---</td>
<td>---</td>
<td>3/6</td>
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<td></td>
</tr>
<tr>
<td>III</td>
<td>5/8</td>
<td>1/8</td>
<td>2/8</td>
<td>---</td>
<td>1/8</td>
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</tr>
<tr>
<td>(n=8)</td>
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</tr>
<tr>
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<td>3/8</td>
<td>1/8</td>
<td>2/8</td>
<td>---</td>
<td>1/8</td>
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<tr>
<td>V</td>
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<td>4/13</td>
<td>2/13</td>
<td>1/13</td>
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</tr>
<tr>
<td>Groups</td>
<td>No. of Cases with Lesions</td>
<td>Esophagus</td>
<td>LES</td>
<td>Cardia</td>
<td>Fundus</td>
<td>Antrum, Pylorus</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------</td>
<td>-----------</td>
<td>-----</td>
<td>--------</td>
<td>--------</td>
<td>----------------</td>
</tr>
<tr>
<td>I (n=10)</td>
<td>---</td>
<td>Pale pink collapsed</td>
<td>---</td>
<td>Pink Rosette like</td>
<td>---</td>
<td>Dark pink</td>
</tr>
<tr>
<td>II (n=6)</td>
<td>1</td>
<td>Pale</td>
<td>Erosions in caudal esophagus</td>
<td>Hyperemia</td>
<td>---</td>
<td>Dark pink</td>
</tr>
<tr>
<td>III (n=8)</td>
<td>2</td>
<td>Pale pink</td>
<td>Erosions in caudal esophagus</td>
<td>Hyperemia</td>
<td>---</td>
<td>Dark pink</td>
</tr>
<tr>
<td>IV (n=8)</td>
<td>2</td>
<td>Pale pink</td>
<td>Erosions</td>
<td>Hyperemia</td>
<td>Erosions (Gastric reflux?)</td>
<td>Dark pink</td>
</tr>
<tr>
<td>V (n=13)</td>
<td>6</td>
<td>Pale Mucosal irregularity</td>
<td>Erosions</td>
<td>Hyperemia</td>
<td>Erosions (Gastric reflux?)</td>
<td>Dark pink</td>
</tr>
</tbody>
</table>
TABLE - 7

*Helicobacter spp.* Isolation and Identification

<table>
<thead>
<tr>
<th>Groups</th>
<th>RUT</th>
<th>Culture</th>
<th>Histopathology</th>
</tr>
</thead>
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<tr>
<td>I (n=10)</td>
<td>3</td>
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<td>---</td>
</tr>
<tr>
<td>II (n=6)</td>
<td>1</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>III (n=8)</td>
<td>4</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>IV (n=8)</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>V (n=13)</td>
<td>8</td>
<td>3 (1)*</td>
<td>3 (1)**</td>
</tr>
</tbody>
</table>

* Out of 3 positive culture results one was negative in histopathology

** Out of 3 positive histopathology results one was negative in culture
CHAPTER – V
DISCUSSION

The study entitled, Endoscopic evaluation of gastrointestinal tract in canine renal failure was undertaken in Small Animal Referral Clinic of Madras Veterinary College Hospital campus with the idea of studying the incidence of gastrointestinal complications in canine renal failure, identifying the nature and extent of gastrointestinal complications and to evaluate the efficiency of Gastroduodenoscopy in identifying the gastrointestinal complications of canine renal failure.

The qualitative and quantitative assessments for the parameters under study were presented in tables/figures wherever necessary and critically discussed.

5.1. INCIDENCE

5.1.1. Age

The age wise incidences of renal failure in 35 dogs selected for the present study are given in Fig.2. Out of thirty-five dogs with renal failure, eight were below five years (22.86%), twelve were between five to ten years (34.29%) and fifteen were above ten years (42.85%). The higher incidence of renal failure in older dogs was reported by Cowgill and Spangler (1981) who recognized renal failure as an important cause of morbidity and mortality in geriatric dogs, as the aging kidney is subject to a variety of morphologic and functional modifications. Several studies in human and rats supported these findings (Darmady et al., 1973; Dunnill and Halley, 1973 and Goldman, 1977). The higher incidence of renal failure in dogs older than ten years was also reported by Polzin et al.,(1995).
5.1.2. Breed

The incidences of renal failure in different breeds of dogs selected for this study are given in Fig. 3. Out of thirty-five dogs, Labrador retrievers showed a higher incidence around 25.72 per cent, German Shepherds 20.00 per cent, Non descripts 17.14 per cent, Spitz 17.14 per cent, Lhasa - Apsos 11.14 per cent, Great Dane 5.71 per cent, and Rajapalayam 2.86 per cent. Cowgill and Spargler (1981) stated that the renal failure is not limited to any breed of dog. A high prevalence of renal failure in Labrador, German shepherd and Non-descripts in the present study may be due to higher percentage of these breeds among the canine population in and around Chennai.

5.1.3. Sex

The sex wise incidences of renal failure in dogs selected for this study are given in Fig. 4. Out of thirty-five dogs selected for this study male dogs constituted 54.29 per cent and female dogs constituted 45.71 per cent. This higher prevalence of renal failure in male dogs may be due to the preference of the pet owners to male dogs in this locality.

5.2. GASTROINTESTINAL SIGNS NOTICED IN CANINE RENAL FAILURE

The gastrointestinal signs noticed in the thirty-five dogs selected for the present study are given in Fig. 1. In the present study anorexia was recorded in 29 dogs (82.86%), which may be due to variety of reasons like polyuria, polydipsia, hypokalemia, metabolic acidosis, non regenerative anemia, hypergastrinemia, secondary hyperparathyroidism, uremic toxins, gastric hyperacidity etc. (Krawiec, 2000). Vomiting was recorded in 26 dogs (74.29%) out of which ten dogs (38.46%) had yellowish vomitus, six dogs (23.08%) had whitish vomitus, eight dogs (30.77%) had brownish vomitus and two dogs (7.69%) had hematemesis. This concurred with Schulman and Krawiec (2000) who recorded
vomiting as a frequent complaint in renal failure due to hypokalemia, acidosis, uremic gastroenteritis and from the effects of uremic toxins on chemo receptor trigger zone. Among the groups studied, 12 dogs in group V (92.31%) had vomiting which concurred with Rubin (1997), who stated that vomiting may not occur until the later stages of chronic renal failure and the severity of vomiting varied with the degree of azotemia. Hematemesis was noticed in two dogs of group V which may be due to gastric ulceration and hemorrhagic diathesis associated with uremia (Polzin and Osborne, 1995). Physical examination revealed halitosis in 18 dogs (51.43%) and oral ulcers in twelve dogs (34.29%). Krawiec (1996) reported that the uriniferous/ammonical breath, stomatitis and mouth ulcers were the common signs of uremia in dogs. The conversion of salivary urea into ammonia by urease-producing bacteria may be responsible for the mouth lesions (Doherty, 1992), poor oral hygiene typical in veterinary patients may exacerbate the onset and severity of uremic stomatitis (Polzin and Osborne, 1995).

Abnormal consistency of motion was observed in twenty-five dogs (71.43%) out of which thirteen dogs (52.00%) had watery motion and twelve dogs (48.00%) had semisolid motion. Abnormal Colour of motion was noticed in twenty dogs (57.14%) out of which twelve dogs (60.00%) had brownish stools and eight dogs (40.00%) had blackish stools. Similar findings were also recorded by Rubin (1997) who opined that hemorrhagic diarrhea might be noticed in severe uremia due to uremic enterocolitis. Brownish and blackish stools observed in the uremic dogs may be due to presence of blood in the stools which may be due to upper gastrointestinal bleeding (Polzin and Osborne, 1995).
Dehydration was noticed in thirty dogs (85.71%) out of which eight dogs (26.67%) had dehydration between six to eight per cent, twelve dogs (40.00%) had dehydration between eight to ten percent, eight dogs (26.67%) had dehydration between ten to twelve per cent and two dogs (6.66%) had dehydration above twelve per cent. These findings concurred with Polzin et al. (1995) who stated that dehydration indicated by dry mucous membranes, decreased skin turgor and sunken eye balls was a common physical finding in dogs with chronic renal failure.

5.3. ERYTHRON

The mean ± S.E. values and F – ratio for erythron of group I, group II, group III, group IV and group V are given in Table 1. The mean ± S.E. values of hemoglobin recorded in the five groups were 14.10 ± 0.34 g/dl, 10.25 ± 1.81 g/dl, 12.19 ± 0.93 g/dl, 9.35 ± 1.29 g/dl and 7.10 ± 0.65 g/dl respectively. Coles (1986) quoted a reference value for hemoglobin ranging from 12 to 18 (15) g/dl. The hemoglobin values recorded in control group (group I, 14.10 ± 0.34 g/dl) were within the normal range as quoted by Coles (1986). A highly significant decrease in hemoglobin values were observed in group II, group IV, and group V and non-significant decrease in group III was observed when compared to control group. McIntyre (1954) noted the presence of anemia in 57 per cent of animals with chronic renal failure and in 20 per cent of animals suffering from the most severe form of primary renal failure.

Anemia recorded in group II, group IV and group V may be due to gastrointestinal hemorrhage with hematemesis or melena, bleeding from the gums or hemorrhage subsequent to venipuncture. Gastrointestinal hemorrhage in patients with
renal failure results from decreased platelet function and abnormalities in the interaction of platelets and vessel walls (Eschbach and Adamson, 1991)

The mean ± S.E values of packed cell volume recorded in the five groups were 44.00 ± 1.33 per cent, 38.17 ± 6.78 per cent, 40.63 ± 2.29 per cent, 31.00 ± 4.33 per cent and 25.39 ± 2.15 per cent respectively. Normal values of PCV in dogs differed widely between 35 to 65 percent (Kerr, 1989). The packed cell volume recorded in control group (group I, 44.00 ± 1.33 per cent) were well within the normal range. A non significant decrease in packed cell volumes were observed in group II and group III and a highly significant decrease in packed cell volume were observed in group IV and group V when compared to the control group indicating the presence of anemia in all four groups with more severe anemia in group IV and group V, this was in agreement with Coles (1986) who opined that the degree of anemia is dependent upon the severity of uremia.

The mean ± S.E. values of red blood cell count recorded in all five groups were 6.13 ± 0.16 million/cu.mm, 5.64 ± 0.99 million/cu.mm, 5.86 ± 0.33 million/cu.mm, 4.84 ± 0.60 million/cu.mm and 4.29 ± 0.32 million/cu.mm respectively. A significant decrease in red blood cell count was observed in group V and a non significant decrease in group II, group III and group IV was observed when compared to control group. Benjamin (1985) quoted a reference value for erythrocyte count ranging from 5.22 to 8.46 million/cu.mm. The values obtained in group I were within the normal range. Coles (1986) reported the presence of borderline anemia in animals not having severe uremia to total erythrocyte count as low as 3 million/µl in animals with severe uremia. A highly significant decrease in hemoglobin, packed cell volume and red blood cell counts in-group V was in agreement in Coles (1986).
5.4. ERYTHROCYTE INDICES

The mean ± S.E. values and F – ratio of MCV, MCH and MCHC in all five groups are given in Table 2.

The mean ± S.E. values of MCV recorded in all five groups were 68.09 ± 1.66 fl, 68.42 ± 2.73 fl, 69.71 ± 2.36 fl, 63.41 ± 2.96 fl and 60.97 ± 2.66 fl respectively. The mean ± S.E. values of MCH recorded in all five groups were 21.98 ± 0.97 pg, 18.60 ± 1.21 pg, 20.85 ± 1.17 pg, 21.26 ± 2.42 pg and 17.38 ± 0.98 pg respectively. The mean ± S.E. values of MCHC recorded in all five groups were 33.44 ± 0.98 per cent, 32.57 ± 0.22 per cent, 31.94 ± 0.66 per cent, 31.58 ± 0.19 per cent and 31.42 ± 0.31 per cent respectively. There was no significant difference in the erythrocyte indices of all five groups.

Coles (1986) recorded the normal values for MCV, MCH and MCHC in dogs as 60 to 77 fl, 20 to 25 pg and 31 to 34 per cent. The values of erythrocyte indices in all five groups were well within the normal ranges indicating the presence of normocytic normochromic anemia.

Coles (1986) reported the presence of normocytic normochromic anemia in dogs with uremia resulting from shortened life span of erythrocytes and failure of erythrocyte production due to diminished erythropoietin synthesis by the diseased kidneys and also stated that there appears to be some correlation between severity of anemia and the degree of elevation of blood urea nitrogen values. The decrease in total erythrocyte count in group V may be due to shortened red cell life span, nutritional abnormalities, erythrocytic inhibitor substances in uremic plasma, blood loss and myelofibrosis (Polzin et al., 1995), erythropoietin deficiency has clearly
emerged as the principal cause of anemia in humans and animals with chronic renal failure (Cowgill, 1992). Several hypotheses have been proposed to account for the erythropoietin deficiency in chronic renal failure: 1. decreased renal mass resulting in an insufficient cellular capacity for new hormone synthesis, 2. lowered set point for response to hypoxic stimulus, and 3. Increased proteolytic activity resulting in accelerated erythropoietin degradation (Hocking, 1987). Severe anemia recorded in group V in the present study may be due to gastrointestinal hemorrhage (Eschbach and Adamson, 1991), shortened red cell life span, nutritional abnormalities, erythropoietic inhibitor substances in uremic plasma, blood loss and myelofibrosis (Polzin et al., 1995). Erythropoietin deficiency has clearly emerged as the principal cause of anemia in humans and animals with chronic renal failure (Cowgill, 1992).

5.5. LEUKOGRAM

The mean ± S.E. values and F – ratio of Leukogram in all five groups are given in Table 3.

The mean ± S.E. values of white blood cell count in all five groups were 8160.00 ± 384.77 /cu.mm, 16083.83 ± 8012.67 /cu.mm, 22562.50 ± 8428.48 /cu.mm, 17875.00 ± 2953.86 /cu.mm and 23969.23 ± 4084.92 /cu.mm respectively. No significant difference in white blood cell count was observed between the groups. Coles (1986) reported that the normal total white blood cell count was 6000 to 15000 /cu.mm. and total white blood cell count >15000 indicated leukocytosis. A non significant increase in total white blood cell counts in group II, group III, group IV when compared to the control group indicated the presence of leukocytosis in all clinical groups.
The mean ± S.E. values of neutrophils in all five groups were 5787.00 ± 327.35 /cu.mm, 7384.67 ± 1978.30 /cu.mm, 18325.00 ± 7472.59 /cu.mm, 14111.38 ± 2804.00 /cu.mm and 20043.69 ± 3606.65 /cu.mm respectively. Coles (1986) reported that the total neutrophils count above 11,800 indicated neutrophilia. A significant increase in neutrophil count in group III and group V and a non-significant increase in neutrophil count in group IV indicated neutrophilia according to Coles (1986).

The mean ± S. E. values of lymphocytes in all five groups were 2196.40 ± 123.95 /cu.mm, 7954.00 ± 5578.57 /cu.mm, 3656.75 ± 725.83 /cu.mm, 3240.88 ± 507.50 /cu.mm and 3207.23 ± 894.50 /cu.mm respectively. The mean ± S.E. values of monocytes in all five groups were 149.10 ± 41.75 /cu.mm, 705.33 ± 537.27 /cu.mm, 239.50 ± 91.64 /cu.mm, 207.25 ± 113.87 /cu.mm and 486.62 ± 136.60 /cu.mm respectively. The mean ± S.E. values of eosinophils in all five groups were 27.50 ± 21.28 /cu.mm, 39.33 ± 26.74 /cu.mm, 416.25 ± 330.01 /cu.mm, 315.50 ± 183.07 /cu.mm and 230.92 ± 101.68 /cu.mm respectively. No significant difference in lymphocyte, monocyte and eosinophil count was observed between all five groups.

In Leukogram neutrophilic leukocytosis observed in group III, group IV and group V when compared to control group were in accordance in Osborne et al. (1972), Chew and Dibartola (1986). Coles (1986) opined that the neutrophilic leukocytosis in uremic patients may be due to stress reaction.

5.6. SERUM BIOCHEMICAL PROFILE

The mean ± S.E. values and F – ratio of serum biochemical profile are given in Table 4.
5.6.1. Serum urea nitrogen

The mean ± S.E. values of serum urea nitrogen recorded in all the five groups were 12.00 ± 1.19 mg/dl, 28.33 ± 4.77 mg/dl, 75.90 ± 4.45 mg/dl, 122.00 ± 4.06 mg/dl and 265.55 ± 30.52 mg/dl respectively. Kaneko (1980) and Coles (1983) reported the normal blood urea levels as 10-28 mg/dl and 10-20 mg/dl respectively. The serum urea nitrogen values recorded to control group were was within the normal range quoted by Kaneko (1980) and Coles (1983). A highly significant increase in serum urea nitrogen values were observed in group IV and group V and a non significant increase in serum urea nitrogen values were observed in group II and group III when compared to control group. Finco and Duncan (1976) reported the elevated mean Blood Urea Nitrogen (BUN) values as 89. ± 11.8 mg/dl, 140 ± 11.6 mg/dl and 194 ± 15.3 mg/dl in prerenal, renal and post renal uremia in dogs. According to Doxey (1983) elevated blood urea levels above 10 m.mol/L should be regarded as indicative of some impairment of renal function and levels above 20 m.mol/L were extremely serious. Chew and DiBartola (1986) demonstrated the relationship of blood urea nitrogen concentrations to the percentage of functional nephrons.

Though the Serum Urea Nitrogen values observed in group I (28.33 ± 4.77 mg/dl) were within the normal range quoted by Kaneko (1980) and do not differ significantly from control group the creatinine values observed in this group was 3.30 ± 0.87 mg/dl. Jackson (1964) stated that the normal creatinine values for dogs as 1-2 mg/dl, while a level of 2-5 mg/dl was indicative of guarded prognosis, 5-7 mg/dl a poor prognosis and above 7 mg/dl an unfavourable prognosis. Polzin et al. (1995) opined that serum creatinine measurements more accurately reflect changes in renal function and so many
extra renal factors influence blood urea nitrogen concentration in patients with chronic renal failure. The serum urea nitrogen values group II, group III, group IV and group V were in agreement with the above authors.

5.6.2. Serum creatinine

The mean ± S.E. values of serum creatinine in all five groups were 0.83 ± 1.13 mg/dl, 3.30 ± 0.87 mg/dl, 3.25 ± 0.28 mg/dl, 5.54 ± 1.33 mg/dl and 7.60 ± 1.07 mg/dl respectively. Jackson (1964) and Richards and Hoe (1967) reported the normal creatinine values in dogs falls within the range of 1.0 to 2 mg/dl. The serum creatinine values in control group were within the normal range quoted by the above authors.

A highly significant increase in serum creatinine values were observed in group IV and group V and non significant increase in serum creatinine values were observed in group II and group III when compared to control group. Jackson (1964) stated that the creatinine value of 2-5 mg/dl was indicative of guarded prognosis, 5-7 mg/dl poor prognosis and above 7 mg/dl, an unfavourable prognosis. Richards and Hoe (1967) opined that the creatinine levels of 4-5 mg/dl were considered indicative of serious renal damage and levels above 7.5 mg/dl were critical. The serum creatinine values in group II, group III, group IV and group V were in agreement with the above authors.

5.6.3. Total protein, albumin and globulin

The mean ± S.E. values of total protein in all five groups were 7.08 ± 0.19 g/dl, 7.05 ± 0.25 g/dl, 6.70 ± 0.17 g/dl, 5.31 ± 0.79 g/dl and 6.08 ± 0.33 g/dl respectively. No significant difference in total protein values were observed in group II and group III and a significant decrease in total protein values was observed in group IV and group V when compared with the control group. Chew and Dibartola (1986) reported that the normal
serum total protein levels in healthy dogs were 5.7 to 7.8 g/dl. Dogs in control group had total protein values well within the normal range quoted by Chew and Dibartola (1986). Though the total protein values in group IV and group V were within the normal range, a statistically significant decrease in total protein values were observed when compared to the control group. This was in agreement with Wiseman et al. (1980) who reported reduced serum protein levels in glomerulonephritis, amyloidosis and nephrosis due to urinary protein loss.

The mean ± S.E. values of albumin values in all five groups were 4.08 ± 0.16 g/dl, 3.67 ± 0.14 g/dl, 3.05 ± 0.24 g/dl, 2.51 ± 0.40 g/dl and 2.07 ± 0.14 g/dl respectively. No significant difference in serum albumin values were observed in group II and highly significant decrease in serum albumin values was observed in group III, group IV and group V when compared with the control group. The serum albumin level in dogs is 3.1 to 4.0 g/dl (Coles, 1986). The albumin value recorded in the control group was well within the normal range. Bush (1983) reported reduced serum albumin levels in renal failure cases caused by an increased filtration of albumin through the glomerulus, owing to its molecular size. Benjamin (1985) attributed reduced albumin levels to inhibition of protein synthesis, increased protein catabolism due to stress, leakage of albumin through the damaged vessels and tissues and as a secondary response to increased globulin concentration. The reduced albumin levels in group III, group IV and group V were in accordance to Bush (1983) and Benjamin (1985).

The mean ± S.E. values of globulin values recorded in all five groups were 3.00 ± 0.08 g/dl, 3.37 ± 0.30 g/dl, 3.65 ± 0.14 g/dl, 2.80 ± 0.53 g/dl and 3.05 ± 0.30 g/dl respectively. No significant difference in serum globulin values were observed in group
II, group III, group IV and group V when compared to the control group. Kaneko (1980) reported the normal globulin values in dogs as 2.1 – 3.7 g/dl. The globulin values recorded in all five groups were in agreement with Kaneko (1980). The comparatively large size of globulin molecule hindered its excretion through the glomerulus thus resulting in normal serum globulin level (Bush, 1983).

5.6.4. Serum potassium

The mean ± S.E. values of serum potassium values in all five groups are 4.18 ± 0.34 mEq/L, 4.52 ± 0.18 mEq/L, 4.33 ± 0.21 mEq/L, 3.97 ± 0.45 mEq/L and 4.41 ± 0.37 mEq/L respectively. No significant difference in serum potassium values was observed between all five groups. Kaneko (1980) and Waterman (1984) reported that the normal potassium levels in dogs as 3.7 to 5.8 mEq/L.

In patients with chronic renal failure, the residual nephrons maintain potassium balance by increasing fractional excretion of potassium in proportion to the decline in glomerular filtration rate by enhancing distal tubular secretion of potassium (Polzin et al., 1995).

5.6.5. Serum phosphorus

The mean ± S.E. values of serum phosphorus values in all five groups are 4.71 ± 0.31 mg/dl, 4.55 ± 0.21 mg/dl, 4.56 ± 0.20 mg/dl, 4.33 ± 0.68 mg/dl and 5.39 ± 0.57 mg/dl respectively. No significant difference in serum phosphorus values was observed between all five groups. The serum phosphorus levels in healthy dogs were 2.6 – 6.2 mg/dl (Kaneko, 1997). Polzin and Osborne (1995) recorded normal phosphorus levels in dogs with chronic renal failure and attributed it to renal adaptive changes.
This adaptive phenomenon is largely an effect of renal secondary hyperparathyroidism as increased parathyroid hormone levels promotes renal excretion of phosphate by reducing the tubular transport maximum for phosphate reabsorption in the proximal tubules by the way of adenyl cyclase system (Polzin and Osborne, 1995).

5.7. URINALYSIS

A moderate proteinuria (++) with epithelial cell casts was observed in four animals of group IV. A severe proteinuria (+++) with epithelial cell casts and pus cells was observed in four animals and severe proteinuria (+++) with pus cells was observed in three animals in group V.

Dibartola (1995) opined that the presence of proteinuria with renal epithelial cell casts was suggestive of acute tubular necrosis or pyelonephritis and white cell or pus casts suggestive of pyelonephritis.

5.8. FECAL OCCULT BLOOD TEST

A positive occult blood result was noticed in one dog from group II and group III three dogs from group IV and six dogs from group V respectively. This finding correlated with the presence of gastric lesion on gastroduodenoscopic examination. Burrows (1986) opined that melena might be observed if bleeding is severe in peptic ulceration in dogs. DiBartola (1995) stated that occult blood test should be interpreted along with urinary sediment examination.

5.9. NEPHROSONOGRAPHY

The nephrosonographic findings in control and clinical cases are summarized in Table 5.
In control group the sonographic architecture presented a complex picture containing a mixture of hyperechoic, hypoechoic and anechoic patterns. The major regions of the kidney included the echogenic cortex, the less echogenic medulla, and the hyperechoic renal pelvis. The areas of the kidney could be ranked in decreasing order of echogenicity as follows, 1. Capsule, 2. Diverticula and vasculature, 3. Renal sinus, 4. Cortex and 5. Medulla. These findings were in agreement with Walter et al. (1987); Konde et al. (1984); Konde (1985); Wood and McCarthy (1990) and Nyland et al. (1995).

Corticomedullary distinction (C/M distinction) was not clear in three animals in group II, five animals in group III, three animals in group IV and six animals in group V.

Corticomedullary distinction was absent in one animal in group IV and six animals in group V.

Walter et al. (1988) reported increased overall echogenicity and reduced corticomedullary definition in dogs with chronic inflammatory diseases and end stage renal disease. End stage kidneys are typically small, irregular and diffusely echogenic with poor visualization of corticomedullary junction and internal renal architecture.

Ultrasonographic abnormalities associated with glomerulo/interstitial nephritis include mild to moderate cortical hyperechogenicity and decreased corticomedullary demarcation (Nyland et al., 1995).

Hyperechoic cortex was observed in one animal in group III two animals in group IV and two animals in group V.

Hricak et al. (1982), Rosenfield (1982) and Stanley et al. (1984) reported an increased cortical echogenicity with enhanced corticomedullary definition in acute or
chronic glomerulonephritis, acute tubular necrosis, leukemic infiltration, amyloidosis etc. due to deposition of collagen or calcium in the renal cortex.

Grooters and Biller (1995) stated that the hyperechogenicity of the renal cortex and the medullary rim sign are the two common sonographic findings in the diffuse parenchymal diseases of kidney.

Hyperechoic medullary rim sign was observed in two animals of group III and one animals in group V.

Biller et al., (1992) reported an outer medullary linear echogenic zone (renal medullary rim sign) in wide variety of pathologic renal lesions ranging from acute tubular necrosis. Pyogranulomatous vasculitis due to chronic interstitial nephritis and in hypercalcemic nephropathy. Ambrust et al. (2001) reported medullary rim sign in cases of leptospirosis.

Medullary band or hyperechoic medulla was observed in one animal in group IV.

Nyland et al. (1995) reported that hyperechoic band at the corticomedullary junction seen with various forms of acute or chronic nephritis and may be related to vasculitis. Forrest et al. (1998) reported that the hyperechoic band was associated with hemorrhage, congestion, edema and necrosis of kidney in leptospirosis.

A normal sonographic picture was identified in three animals in group II and one animal in group IV. A normal ultrasonographic picture does not entirely rule out renal disea (Walter et al., 1987).
5.10. ENDOSCOPY

5.10.1 Gastroduodenoscopy

The gastroduodenoscopic findings in control and clinical cases are summarized in Table 6.

5.10.1.1. Esophagoscopy

In the control group the esophagus was found collapsed and upon insufflation the mucosa was pale pink with fine submucosal vessels. The lower esophageal sphincter was closed and had an irregular rosette appearance. These findings were in agreement with Tams (1990).

In group II one case had a pale esophageal mucosa with erosions in caudal esophagus. Similarly pale pink mucosa with erosions in the esophagus was observed in two cases in group III and group IV respectively. In group V pale esophageal mucosa, mucosal irregularity and erosions was noticed in six cases. Sullivan and Miller (1985) noticed friable mucosa, hyperemia and erosions in esophageal mucosa in gastroesophageal reflux. Tams (1990) observed mucosal irregularity and erosions in esophagitis.

5.10.1.2. Lower esophageal sphincter (LES)

In control groups the lower esophageal sphincter was closed and had an irregular rosette appearance. One animal in group II and two animals in group III showed hyperemic changes in LES. Two animals in group IV and six animals in group V showed hyperemic changes and erosions (gastric reflux?) in LES (Plate ). Lane (1981) concluded that reflux esophagitis may be confirmed by fibroptic examination of the esophagus.
Tams (1990) recorded erythema and erosions in LES in patients with gastroesophageal reflux disorders.

### 5.10.1.3. Cardia

The cardia of the stomach was uniformly dark pink and no lesions were found in cardia of animals in all five groups. O'Brien (1980) opined that the normal gastric mucosa in dogs is uniformly bright red.

### 5.10.1.4. Fundus

In control and group I animals after entering into fundus the mucosa was dark pink, rugal folds were noticed on the greater curvature. On insufflation the rugal folds began to separate. These findings were in agreement with Tams (1990).

Two animals in group III, two animals in group IV and six animals in group V showed hyperemic changes and linear erosions in the fundus. Tams (1990) observed mucosal erythema and multifocal erosions of fundus in chronic gastritis.

### 5.10.1.5. Antrum and pylorus

In control animals there were no rugal folds and peristaltic contractions observed in the antrum which concurred with Tams (1990).

In group II one animal showed linear erosions in pyloric antrum. In group III two animals had bile in the antrum. Two animals in group IV and six animals in group V had erosions and bleeding ulcers in the pyloric antrum. Kavitha (1997) observed shallow ulcers, invasive erosions and old spots of hemorrhage more frequently in antrum and pylorus in uremic dogs.
5.10.1.6. Duodenum

In control animals the duodenum was pink, smooth and uniform which concurred with Obrien (1980). Two animals in group IV and six animals in group V had erosions and ulcers in duodenum. Thickening of the duodenal wall and duodenal ulcers have been documented in a dog during endoscopic examination of duodenum (Happe and Gaag, 1983).

In the present study one dog in group II had erosions in caudal esophagus, linear erosions and ulcers in antrum and pylorus and erosion in duodenum. Two dogs in group III and group IV had erosions in esophagus LES and antrum and ulcers in duodenum. Six dogs in group V had mucosal irregularity and erosions in esophagus, LES and fundus and erosions and ulcers in pylorus and duodenum. The severity of mucosal lesions varied with the level of azotemia. Bleeding ulcers in pyloric antrum and duodenum were recorded in group IV and group V. Kavitha (1997) reported that the severity of mucosal lesions increased with the degree of azotemia in dogs.

Gross anatomic abnormalities including gastritis, ulceration and hemorrhage had been reported by several authors in uremic dogs (Lazarus, 1991; Polzin and Osborne, 1995; Krawiec, 1996; Schulman and Krawiec, 2000). Kavitha (1997) endoscopically, recorded hemorrhagic type of ulcerative gastritis in uremic dogs.

5.10.2 Histopathology of endoscopy guided mucosal biopsy

Endoscopy guided mucosal biopsy was done on the lesion sites in animals with lesions and random biopsies of pyloric antrum in animals without lesions were taken. Histopathological examination of these biopsies was done.
In group II three animals showed mild fibrosis of lamina propria, mild submucosal fibrosis and distension of gastric glands, one dog showed submucosal fibrosis and hemorrhage respectively.

In group III two animals had submucosal fibrosis, atrophy of gastric glands with mononuclear cell infiltration, one animal showed submucosal fibrosis with increased goblet cell activity.

In group IV two dogs had increased goblet cell activity, submucosal hemorrhage, one dog had submucosal fibrosis and one dog had mucosal hyperplasia.

In group V six dogs revealed severe fibrosis and ulceration, two dogs with more severe fibrosis and ulceration, three dogs showed hyperplastic changes, one dog showed atrophy of gastric glands, one dog had ulceration, submucosal congestion and fibrosis and one dog had glandular hyperplasia with mononuclear cell infiltration.

Microscopic changes including glandular atrophy, edema of lamina propria, mast cell infiltration, fibroplasias, mineralization and submucosal arteritis had been reported by several authors in uremic dogs (Lazarus, 1991; Polzin and Osborne, 1995; Krawiec, 1996; Schulman and Krawiec, 2000).

Shousha et al. (1989) reported 59 per cent incidence of chronic duodenitis and 62.5 per cent incidence of gastric metaplasia in human patients with chronic renal failure. 40 per cent of people with renal failure reportedly have gastrointestinal complications. Mucosal lesions of gastritis and duodenitis are most commonly seen on endoscopic evaluation of human patients with renal failure (Krawiec, 1996). Out of 35 clinical cases, 11 dogs (31.11%) showed mucosal abnormalities in gastroduodenoscopic examination and 24 dogs (60.80%) showed mucosal abnormalities in endoscopy guided
mucosal biopsy specimen, which clearly indicates the need for histopathological examination of mucosal biopsy specimen even in the absence of endoscopic abnormalities. Several authors reported that that the mucosa can appear endoscopically normal inspite of the presence of significant inflammatory or neoplastic disease (Roth et al., 1990 and Dennis et al., 1992).

**5.11. ISOLATION OF HELICOBACTER SPP.**

The results of isolation of gastric *Helicobacter spp.* by rapid urease testing, culture and histopathology are summarized in Table-7.

**5.11.1. Rapid urease test (RUT)**

Three dogs in control group, one dog in group II, four dogs in group III, three dogs in group IV and eight dogs in group V had a positive result in rapid urease testing.

Sensitivity and specificity of RUT had been validated by many studies (Marshal *et al.*, 1987 and Chu *et al.*, 1997). The sensitivity and specificity of RUT were 90.2 per cent and 100 per cent respectively in human patients with *H. pylori* infection (Megraud, 1996). False positive and false negative results are common RUT. The sensitivity of the test depends upon the number of bacteria in the biopsy. It has been calculated that $10^4$ organisms are required for a positive result (Bourguignon, 1989). Treatment with anti *Helicobacter spp.* drugs or antisecretary drugs reduce the density of bacteria and is therefore associated with decreased sensitivity of RUT (Chu *et al.*, 1997), which may contribute to false negative results. Strauss-Ayali and Simpson (1999) opined that the other urease producing bacteria in the stomach (eg. *Proteus mirabilis*) can give false positive results.
5.11.2. Culture of *Helicobacter* spp.

The *Helicobacter* spp. organisms were isolated and identified in cultures of one dog from group IV and three dogs from group V. Out of these three dogs in group V, one dog had a negative result in histopathology.

Fox (1998) opined that a definitive diagnosis requires culture and isolation of the specific species of Helicobacter and stated that the culture and isolation of common gastric spiral organisms like *H. bizzozeronii* and *H. felis* was extremely difficult. Eaton *et al.* (1996) concluded that the culture has low sensitivity (15.4% - 51.0%) when compared to other diagnostic methods.

Yachha *et al.* (1996) in their study on *Helicobacter pylori* infection in children with portal hypertensive gastropathy in which culture, RUT and histology were used for the diagnosis of *H. pylori* infection, culture gave poor results. Ghoshal and Guha Mazumder (1999) opined that the culture is limited to some of the research laboratories and is rarely available for routine clinical use and stated that culture can be used for knowing the drug sensitivity pattern of the organism.

5.11.3. Histopathologic findings

5.11.3.1. Detection of *Helicobacter* spp.

*Helicobacter* spp. were identified in one dog in group IV and three dogs in group V. The bacteria were practically unidentifiable by H & E staining. Similar difficulties were recorded by Strauss-Ayali and Simpson (1999) who recommended silver stains such as Warthin-Starry stain and modified Steiner stain for reliable detection of spirochetes in gastric biopsies. However, Happonen *et al.* (1996) described similar efficacy with H & E stain compared to Warthin-Starry stain and Warthin-Starry stain was found to be superior
in only 1 of 30 samples taken from dogs that were evaluated. Stevens and Francis (1996) recommended the Toluidine blue in Sorenson’s buffer for staining *Helicobacter spp.* and stated that these organisms appeared dark blue against variable blue background.


### 5.11.3.2. Histopathologic changes

The histopathologic changes in the gastric mucosal biopsy samples stained with H & E was correlated with the identification of *Helicobacter spp.* in the same biopsy samples stained with Toluidine blue in Sorenson’s buffer. One dog in group IV with *Helicobacter* associated gastritis had increased goblet cell activity and submucosal hemorrhage. Among the three dogs with *Helicobacter* associated gastritis in group V one dog had severe fibrosis and ulceration, one dog had chronic gastritis with atrophy of gastric glands and one dog had glandular hyperplasia with mononuclear cell infiltration.

The variability of histopathological criteria used in individual studies and the lack of a standardized canine – based grading system for gastric histopathological changes make comparison of histopathological results between studies difficult (Strauss-Ayali and Simpson, 1999).

Poutahidis *et al.* (2001) made a comparison of histopathological changes with the detection of *H.pylori* in experimentally induced gastritis in conventional piglets to establish animal model for human *H.pylori* associated gastritis.
In RUT three dogs from group I, one dog from II, four dogs from group III, three dogs from group IV and eight dogs from group V has positive results. This higher incidence of *Helicobacter* spp. detected by RUT may be due to high prevalence of *Helicobacter* organisms in clinically normal and as well as abnormal dogs (Yamasaki et al., 1998). Other urease producing bacteria in the stomach such as *Proteus mirabilis* may also contribute to false positive results (Strauss-Ayali and Simpson, 1999).

Out of 35 clinical cases one dog in group IV and two dogs in group V had positive results in both culture and histopathology. In group V, one dog showed positive result in culture but *Helicobacter* spp. was not identified in histopathology and one dog has positive result in histopathology but *Helicobacter* spp. failed to grow in culture. The low incidence of *Helicobacter* organisms identified by culture may be due to difficulty in culturing of common *Helicobacter* spp. in dogs, patchy distribution of the organisms, technical factors like delay in transport, prior treatment of the animal with anti – *Helicobacter* and anti - secretary drugs, etc. (Fox, 1998; Strauss-Ayali and Simpson, 1999; and Ghoshal and Guha Mazumder, 1999).

Five *Helicobacter* spp. were identified by culture and histopathology (17.14%). Gastric *Helicobacter* spp. are highly prevalent in dogs and have been identified in 61 per cent to 82 per cent of dogs presented for the investigation of vomiting, in 67 per cent to 86 per cent of clinically healthy pet dogs (Strauss-Ayali and Simpson, 1999) and approaching 100 per cent in laboratory Beagles and shelter dogs (Cornetta et al., 1998).

Several species of canine gastric *Helicobacter* spp. have been cultured, including *H.felis* (Paster et al., 1991), *H.bizzozeronii* (Hanninen et al., 1996) and *H.salomonis*
(Jalava et al., 1997). These three species were common isolates from dogs (Happenen et al., 2000).

Gastric *Helicobacter spp.* have been suspected of inducing histologically verifiable gastritis and degeneration of gastric glands and parietal cells (Henmanns et al., 1995). Studies have so far failed to classify the association of canine gastric *Helicobacter spp.* with gastritis and gastrointestinal signs. Human *H. pylori* had been demonstrated to play an important role in gastritis, gastroduodenal ulceration and gastric cancer (Parsonnet, 1993 and Lambert et al., 1995). It has been shown that eradication of *H. pylori* was more effective in preventing the recurrence of gastroduodenal ulcer (Uemura et al., 1995)

No study has been so far documented regarding the prevalence of *Helicobacter spp.* in antral biopsy samples of dogs with renal failure whereas, *H. pylori* was significantly less in human patients with renal disease (24%) than in control group (42%) (Shousha et al., 1990). Shousha et al. (1989) identified *C. pylori* in only two patients (2.5%) and suggested that the duodenal environment of human patients with chronic renal failure remains hostile to the growth of these organisms. However, Chhina et al. (1998) that 42 per cent of human patients with chronic renal failure were infected with *H. pylori*. Amongst them, the patient with normal endoscopy had a lower prevalence as compared to those with endoscopic changes.

In the absence of other evidences it can be concluded that the prevalence of *Helicobacter spp.* in dogs with renal failure (17.14%) may also be considered in the medical management of dogs with severe azotemia.
5.12. POSTMORTEM FINDINGS

Post mortem examination was conducted in fifteen animals which died. One dog from group II, three dogs from group III, four dogs from group IV and seven dogs from group V died despite treatment.

5.12.1. Gross pathology

A moderate to severe adhesion of the capsule to the cortical surface, pitting and granularity of the cortex were noticed in majority of cases. Irregular cortical surface, a few pale foci of the cortex and congestion of the cortico-medullary junction were also recorded. These findings are in accordance with Confer and Panciera (1997).

5.12.2. Histopathology

In group II kidney showed interstitial fibrosis, tubular epithelial necrosis, atrophy of isolated glomeruli and infiltration of lymphocytes indicating chronic nephritis and stomach showed congestion of lamina propria.

Kidneys of two cased in group III showed homogenous eosinophilic contents in the tubular lumen, atrophic changes of tubular epithelium and plasma cell infiltration.

In group IV kidneys showed calcification of necrotic tubular epithelium, calcification of portion of glomeruli was also evident in two cases, stomach showed hyperplastic reaction indicating chronic gastritis.

In group V kidneys showed necrosis of renal substance indicating suppurative nephritis, the infiltration included lymphocytes and plasma cells in the interstitium, one of the cases showed neutrophilic infiltration. The postmortem findings in kidneys concurred with Center et al. (1987) and Cook and Cowgill (1996).
CHAPTER – VI

SUMMARY AND CONCLUSIONS

The study on “Endoscopic evaluation of gastrointestinal tract in canine renal failure” was conducted at the Centre of Advanced Studies in Veterinary Clinical Medicine, Ethics and Jurisprudence, Madras Veterinary College Hospital on ten apparently healthy dogs and thirty five clinical cases.

The objectives of the study were to study the incidence of gastrointestinal complications in canine renal failure, to study the nature and the severity of gastrointestinal complications in canine renal failure and to evaluate the efficiency of endoscopy in identifying gastrointestinal complications in canine renal failure.

Ten apparently healthy dogs from the Tamil Nadu Commando School, dog squad were selected for obtaining normal data. The dogs presented at the Small Animal Clinic of the Madras Veterinary College Hospital were screened for renal failure. Out of these, thirty five dogs with renal failure diagnosed by history, clinical findings, hematology Leukogram, serum biochemistry, routine urinalysis, fecal occult blood test and nephrosonography were selected as clinical cases. The clinical cases are then grouped based on the degree of azotemia.

The control animals and the clinical cases were allotted into five groups as follows,

Group I  - (n = 10) Control animals
Group II - (n = 6) Mild azotemia (SUN ≤ 50 mg/dl)
Group III - (n = 8) Moderate azotemia (SUN = 50 to 90 mg/dl)
Group IV - (n = 8) Severe azotemia (SUN = 90 to 140 mg/dl)
Group V  - (n= 13) Very severe azotemia (SUN ≥ 140 mg/dl)
Gastroduodenoscopic examination was carried out in the animals of all five groups to detect the mucosal abnormalities. Gastroscopy guided mucosal biopsy was done in all clinical cases regardless of the presence or absence of gastroduodenoscopic abnormalities.

Further, isolation and identification of the *Helicobacter spp.* was attempted in all the clinical cases to detect the prevalence of *Helicobacter spp.* in uremic gastropathy of dogs and to compare the various invasive methods used for the detection of *Helicobacter spp.* in uremic dogs. However, the speciation of these *Helicobacter* organisms was not attempted.

Higher incidence of renal failure was observed in dogs aged above ten years, higher incidences of renal failure were observed in Labrador retrievers, German shepherd, Non-descripts and Spitz and male dogs were affected more commonly than female dogs.

The gastrointestinal signs commonly observed in dogs with renal failure were anorexia, vomiting, oral ulcers, halitosis, abnormal consistency of stools like watery and semisolid stools, abnormal colour of stools like brownish and blackish stools and dehydration. The erythron values and erythrocyte indices revealed the presence of normocytic normochromic anemia in dogs with renal failure and the severity of anemia increased with the elevation of serum urea nitrogen values. The Leukogram neutrophilic leukocytosis was observed in severe and very severe azotemic animals. Serum biochemical profiles revealed significant elevations in total protein and albumins and these variations had some correlation with the degree of azotemia. Moderate to severe proteinuria was observed in severe and very severe azotemia.
Reduced and/or absence of corticomedullary distinction, hyperechoic cortex, hyperechoic medullary rim and hyperechoic medullary band were the consistent nephrosonographic findings in dogs with renal failure.

Gastroduodenoscopic examination with OLYMPUS – Type GF, gastrofibroscope revealed mucosal irregularity and erosions in caudal esophagus, hyperemia and erosions in lower esophageal sphincter, hyperemia and erosions of gastric fundus, erosions and ulcers in pylorus and thickening of duodenal wall and duodenal ulcers. Fibrosis of lamina propria, atropy of gastric glands, increased goblet cell activity, infiltration of lymphocytes and plasma cells, erosions and ulcerations were the consistent findings on histopathological examination of endoscopy guided mucosal biopsy.

As 31.11 per cent of animals showed mucosal abnormalities on endoscopic examination and 60.80 per cent of animal showed mucosal abnormalities on histopathological examination of endoscopy guided mucosal biopsy specimen and hence a normal gastroduodenoscopic finding was unable to rule out the presence of gastric disease. The severity of gastric mucosal changes identified by Gastroduodenoscopy and endoscopy guided mucosal biopsy varied with the level of azotemia. Thus gastroduodenoscopic examination and endoscopy guided gastric mucosal biopsy studies were found to be a semi-invasive, safe, sensitive and reliable method for identifying the gastrointestinal complications of renal failure in dogs. Gastroduodenoscopic examination should be accompanied by endoscopy guided mucosal biopsy studies. However, the need for general anesthesia especially in renal failure patients remained the potential complication during endoscopic examination.
Three dogs of control group and sixteen dogs from clinical cases showed positive results in rapid urease testing. *Helicobacter spp.* was identified in five dogs (17.14%), by culturing of these organisms and by identification of these organisms in gastric mucosal biopsies stained with Toluidine blue in Sorenson’s buffer. This prevalence of *Helicobacter spp.* should be considered in the medical management of dogs with severe and very severe azotemia.

**CONCLUSIONS**

1. Males were predominantly affected than females and the dogs above ten years were most commonly affected and higher incidences was observed in Labrador retriever, German shepherd, Non-descript and Spitz.

2. Out of thirty five dogs evaluated, twenty nine dogs showed anorexia (82.86%), twenty six dogs showed vomiting (74.29%), twenty five dogs showed abnormality in consistency of stools (71.43%), twenty dogs showed abnormality in colour of stools (57.14%), eighteen dogs showed halitosis (51.43%) and twelve dogs had oral ulcers (34.29%).

3. Gastroduodenoscopic abnormalities were found in eleven dogs (31.11 %). Mucosal irregularity and erosions of caudal esophagus, hyperemia of LES, hyperemia and erosions of fundus, erosions and ulcers in pylorus and duodenal ulcers were the consistent findings. Ulcers in the pyloric antrum and duodenum where recorded in dogs with severe and very severe azotemia. Gastroduodenoscopic abnormalities correlated with the degree of azotemia.
4. Mucosal abnormalities were identified in 24 dogs (60.80%) on histopathological evaluation of endoscopy guided mucosal biopsy specimen. Fibrosis of lamina propria, atrophy of gastric glands, increased goblet cell activity, infiltration of lymphocytes and plasma cells, erosions and ulcerations were the consistent findings. Erosions and ulcers of gastric mucosa were noticed in more severe azotemia.

5. Gastroduodenoscopic examination should be accompanied by endoscopy guided mucosal biopsy studies even in the absence of endoscopic abnormalities.

6. The prevalence of Helicobacter spp. were found to be 17.14 per cent in dogs with renal failure, mostly in very severe azotemia. Hence, Helicobacter spp may be considered in the medical management of dogs with severe azotemia.
CHAPTER-VII

REFERENCE


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APPENDIX - 1
PROFORMA FOR CLINICAL STUDY
ENDOSCOPIC EVALUATION OF GASTROINTESTINAL TRACT IN CANINE

RENAL FAILURE

ENDOSCOPY UNIT
SMALL ANIMAL MEDICAL REFERRAL CLINIC
CENTRE FOR ADVANCED STUDIES
IN
VETERINARY CLINICAL MEDICINE, ETHICS AND JURISPRUDENCE
MADRAS VETERINARY COLLEGE HOSPITAL, CHENNAI - 600 007
INDIA

Case Identity: 

Owner identity: 

S.No : _________  Name :____________
Case No: _________  Address:  ___________
Date : ___________  ____________________
_______Ph: _______

SIGNAL MENT
Breed: ____________  Age : _________  Sex:__________
Colour: ____________  B.Wt : _________  Name : ________

HISTORY

1.  Duration of illness_______________________________
2.  Previous illness/injury____________________________
3.  Past history of renal disease; Yes  No
   If Yes, recent evaluation of renal function
   ____________________________
4.  Exposure to possible nephrotoxins Yes  No
    If yes, specify_____________________________
5.  Recent trauma / Surgery / Anestheisa? ____________________
6. **Diet:**
   - Type? ____________
   - Frequency of feeding? ____________
   - Supplements? ________________
   - Recent diet changes? ____________
   - Preferences? ________________

7. **Water consumption:**
   - Increased / Decreased / Not known / No change
   - If change noticed, when? ________________

8. **Micturition:**
   - Frequency? ____________
   - Quantity? ____________
   - Pollakuria (dysuria / tenesmus)? ____________
   - Polyuria? ____________
   - Oluguria? ____________
   - Anuria? ____________
   - Urinary incontinence? ____________
   - Micturition in unusual conditions? ____________
   - Change in urine color?
     - (a) red (hematuria/hemoglobinuria)? ____________
     - (b) Brown / Black / Green / Others? ____________
   - Change in urine odor? Yes [ ] No [ ]
     - If Yes, specify ____________________________
   - Uroliths voided during micturition

**Other signs not directly related to urinary system?**

(i) **Vomiting?** Yes [ ] No [ ]
   - If Yes, color? ____________
   - Quantity? ____________
   - Frequency? ____________
   - Associated with eating ________________________
   - Associated with other signs:
     - Any change, better / worse / same?
     - Medication given? Yes [ ] No [ ]
       - Type ____________, dose ____________, response ____________

(ii) **Diarrhea?** Yes [ ] No [ ]
   - Character? ____________
   - Color? ____________
   - Quantity? ____________
   - Frequency? ____________
   - Any change, better / worse / same?
**Medication given?** Yes ☐ No ☐ If Yes, Type __________, dose __________, response __________

(iii) Anorexia? Yes ☐ No ☐ If Yes, how long?_________

(iv) Wt. Loss? Yes ☐ No ☐ If Yes, specify _______

(v) Others?________________________________________

**PHYSICAL EXAMINATION**

1. Temperature __________

2. Pulse: frequency ______ intensity ______ duration ____ amplitude_____

3. Resp: rate ______ rhythm _____ depth _____ type___________

4. Hydration status dehydrated / nondehydrated
   If dehydrated, specify ___________
   Skin pliability ___________ xerostomia ___________
   CRT ___________

5. Oral Cavity:
   mucosal ulcers? ___________
   discoloration of tongue? ___________
   pallor of mucous membranes? ___________
   evidence of vomitus? ___________
   loose / missing teeth? ___________
   xerostomia? ___________
   uremic breath? ___________

6. Palpation of kidneys:
   both kidneys palpable Yes ☐ No ☐ If Yes, bilaterally symmetric / asymmetric
   position in abdominal cavity? _________________

7. Palpation of bladder?
   Position? _________________
   Size? _________________
   Consistency? ___________ pain? ___________
   Thickness of bladder wall? _________________
   Grating / nongrating masses / adjacent to bladder lumen
   (if present, its location constant / variable __________)
8. Rectal examination:
   Feces normal / abnormal, if abnormal, specify___________
   Prostate gland
   Position? ___________ size? ___________
   Shape? ___________ consistency? ___________
   Pain? ___________

LABORATORY EXAMINATION

1. Hematological profile:
   Erythron & Leukon   Differential count (absolute)
   Hb  _______g/dl  Neutrophils  _________
   PCV  _______%  Lymphocytes  _________
   RBC  ______10^6/ml  Monocytes  _________
   WBC  ______10^3/ml  Eosinophils  _________
   Reticulocyte _______%  Basophils  _________
   Erythrocyte indices:
   MCV _______fl  MCH _______pg  MCHC _______%
   Type of anemia____________________________________

2. Serum chemistry profile:
   BUN _________mg/dl  Creatinine _________mg/dl
   Total protein _______g/dl  Albumin _________g/dl
   Globulin _________ g/dl  A/G ratio _________
   Potassium _______m.Eq./dl  Phosphorous _______mg/dl

3. Urinalysis
   Color _________ Sp.gravity _________
   Reaction _________ Protein _________
   Glucose _________ Ketones _________
   Blood _________ Bile salts _________
   Bile pigments _________ Sediments _________
   Urine protein / Creatinine ratio _________
SPECIAL EXAMINATION

1. Nephrosonography
   Lt. Kidney
   Length _____ Width _____
   C/M distinction __________
   Others ________________
   Rt. Kidney
   Length _____ Width _____
   C/M distinction __________
   Others ________________

2. Gastroduodenoscopy

3. Endoscopy guided mucosal biopsy
   a. Biopsy urease test positive / negative
   b. Culture of Helicobacter
   c. Histopathology

4. Necropsic Renal histopathology
(If applicable)

REMARKS

MAJOR GUIDE

RESEARCH SCHOLAR
APPENDIX - 2

CONSENT FOR ANESTHESIA AND ENDOSCOPIC PROCEDURES

C.No. ______

Description of Patient

Breed : ______ Age : _______ Sex : __________

Color : ______ B.Wt: _______ Name: __________

Owner / Agent

Name : _______________________________________

Address: _______________________________________

_____________________________________________

Telephone: Res__________ Off ___________________

Endoscopic procedure ____________________________

I hereby, give permission for the administration of anesthetics to the above animals and to perform the endoscopic procedure detailed on this form, together with any other procedures which may prove necessary.

I understand that all anesthetic techniques and endoscopic procedures involve some risk to the animal.

I have read and understood this form.
I am over 18 years of age.
I have notified / will notify immediately the insurers concerning the procedures planned for this animal.

Signature of the owner / agent ____________________

Name ____________________ Date ____________
APPENDIX – 3

ACUTE KIDNEY DISEASE

Acute kidney disease is a general term referring to kidney disease of sudden onset. About three fourths of the total kidney tissue must be damaged before signs of illness appear. Kidney disease is often life threatening, as the body cannot eliminate waste products or maintain the balance of fluid and elements vital to life.

Causes of acute kidney disease include infections, poisons, trauma, urinary tract obstructions, and diseases of the immune system. The resulting damage to the kidneys may not be reversible.

Common signs of illness may include depression, lack of appetite, vomiting, diarrhea, increased water consumption, and increased or decreased urine output.

Important Points in Treatment

1. Kidney disease is very serious and hospitalization is usually required. Laboratory tests are necessary for diagnosis and evaluation of the response to treatment.
2. Intravenous fluids are given to improve urine production and restore normal electrolyte and fluid balance.
3. Diet: Follow the instructions checked.
   - Feed the normal diet.
   - A special diet is required. Feed ____________________________________________
   ____________________________________________

4. Provide access to clean, fresh water at all times.
5. Medication: Give all medication as directed. Call the doctor if you cannot give the medication.
6. Activity: Follow the instructions checked.
   - Allow normal activity.
   - Restrict activity as follows: ____________________________________________

Notify the Doctor if Any of the Following Occur

- Your pet refuses to eat.
- Your pet has diarrhea or vomits.
- Your pet becomes depressed.
- Your pet’s signs recur after an apparent recovery.

- A urine sample is requested.

Your next appointment is ________________________________
Normal kidneys filter the blood, removing wastes and excreting them in the urine. Kidneys damaged by infection or inflammation lose some of this filtering ability, and waste products accumulate in the bloodstream. Continued re-circulation of this waste material results in illness. About three fourths of kidney tissue must be damaged before signs of illness appear. For this reason, kidney disease is often considered chronic (presence a long time) even though the affected pet may not have shown signs of disease for very long.

Signs of chronic kidney disease include vomiting, diarrhea, increased thirst, increased urination, decreased appetite, depression, and bad breath. Continued illness results in collapse, seizures, coma, and death.

Although chronic kidney disease is not curable, it is often controllable. Many pets can live reasonably normal lives when properly managed in a cooperative effort between owner and veterinarian.

**Important Points in Treatment**

1. In many cases, initial treatment involves flushing the animal’s blood with intravenous fluids until kidney function improves. Usually this is done in the hospital. When the values of the kidney function tests are more normal, treatment can continue at home.
2. Medication: Give all medication as directed. Call the doctor if you cannot give the medication.
3. Diet: A controlled diet is critical to successful treatment of chronic kidney disease. Feed your pet as follows:

   ______________________________________________________
   ______________________________________________________
   ______________________________________________________
   ______________________________________________________

4. Water: Make sure your pet has free access to clean drinking water at all times. Call the doctor if your pet does not seem to be drinking adequately.
5. Activity: Follow the instructions checked.
6. Activity: Follow the instructions checked.

   _______ Allow normal activity.
   _______ Restrict activity as follows:

**Notify the Doctor if Any of the Following Occur**

- Your pet is reluctant to eat or seems depressed.
• Your pet has diarrhea or vomits.
• Your pet faints or acts dazed or confused.
• There is a change in your pet’s water intake and/or urination.

_________A urine sample is requested.

Your next appointment is ____________________________________________________________