Original Research

Clinical and Haemato-Biochemical Alterations in Canine Renal Dysfunction

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Abstract

The present investigation was conducted with the aim of determining the haemato-biochemical alterations in dogs with renal dysfunction. Of the 170 dogs screened for renal dysfunction 44 dogs (25.88%) were found to be positive for renal dysfunction based on clinical signs and haemato-biochemical changes. The predominant clinical changes associated with renal dysfunction were anorexia, weight loss, weakness, vomiting, emaciation, pale mucous membrane, polyuria, polydipsia, inappetence, recumbency, anuria, halitosis, oral ulcers, epistaxis, seizure and cataract/blindness. Moderate to severe anemia with significant biochemical alterations viz., elevation in BUN, serum creatinine and phosphorous and a non-significant elevation in serum sodium and potassium and fall in total protein and albumin levels were observed in dogs with renal dysfunction. A highly significant increase in urine protein concentration along with significant decrease in urine creatinine concentration was also noted.

Key words: Creatinine, Dog, Haemato-Biochemical, Protein, Renal Dysfunction

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Introduction

Renal dysfunction is among the most common ailments of dogs and contributes substantially to canine mortality, particularly in older dogs and is the third leading cause of death in dogs (Bronson, 1982 and Lund *et al*., 1999). A variety of adverse influences (e.g., toxins, overdosed drugs, infectious agents, ischaemic insults, neoplasia) can damage the kidneys either reversibly or irreversibly to produce renal insufficiency leading to renal failure (Cowgill and Elliot, 2000 and Graner, 2007) and are clinically manifested by change in water intake and in the frequency, colour and volume of urine and associated systemic problems. Renal

dysfunction induces haematological and serum biochemical alterations in affected dogs associated with a variety of haemopoietic changes and can be diagnosed on the basis of hemato-biochemical changes and urine analysis (Kralova *et al*., 2010; Kandula and Karlapudi, 2015; Chhibber *et al*., 2017). With a loss of 67–75% of the filtration rate, severe polyuria and polydipsia occur; when the failure increases (75–90%) the accumulation of blood nitrogen catabolic products determine systemic signs such as anorexia, weight loss and apathy and specific signs such as vomiting and diarrhea. When the residual renal function is less than 10 per cent uremia is present, associated with neurological signs (uremic encephalopathy) that indicate a terminal stage of the illness (Polzin *et al.*, 2000 and Pugliese *et al*., 2005). With an increasing number of renal diseases in the dog population in the north eastern region of India and the lack of documentation of such study from this region prompted us to investigate some of the pertinent haemato-biochemical alterations that occurs in dog suffering from renal dysfunction irrespective of the cause.

Materials and Methods

Present study was carried out at Teaching Veterinary Clinical Complex, College of Veterinary Science, AAU, Khanapara, Guwahati – 22, Assam, India from August 2016 to May 2017. Ten apparently healthy adult dogs of either sex registered for routine annual health check-up were selected as control group and 170 dogs suspected to be suffering from some renal ailments were screened. Confirmation of the dogs suffering from renal dysfunction was done on the basis of the history, detailed physical examination, haematology, serum biochemical profile and urinalysis. Whole blood was collected aseptically from the saphenous or cephalic vein of the dogs into Na_2EDTA vacutainers, clot activator vials and sodium fluoride vials for haematology, biochemical studies and glucose estimation respectively. Blood samples of healthy control as well as dogs with renal dysfunction were subjected to haematological examinations comprising of haemoglobin (Hb) (g/dL), packed cell volume (PCV) (%), total erythrocyte count (TEC) ($\times 10^6/\mu L$), total leukocyte count (TLC) ($\times 10^3/\mu L$) following standard procedures as described by Moritz (2010). Serum samples were subjected to analysis for total protein (TSP), albumin, urea nitrogen (BUN), creatinine, sodium, potassium, phosphorus, calcium and glucose spectrophotometrically using standard kits. Urine samples were collected aseptically by catheterization and subjected to urinalysis and urine biochemistry was done using standard procedures. Urine protein concentration (Dipstick) and creatinine concentration using Modified Jaffe's method, Murrey (1984) were estimated. The data obtained were subjected to statistical analysis using two-way ANOVA by Statistical Analysis Software (SAS Enterprise Guide 9.3 version).

Results and Discussion

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Clinical Signs

Most prominent clinical signs recorded in the present study were anorexia (75%), weight loss (68.18%), weakness (68.18%), vomiting (68.18%), emaciation (61.36%), pale mucous membrane (50%), polyuria (47.72 %), polydipsia (47.72 %), inappetence (31.81%), recumbency (22.72%), anuria (6.81%), halitosis (6.81%), oral ulcers (6.81%), epistaxis (4.54%) seizure (2.27%), congested mucous membrane (2.27%) and cataract/blindness (2.27%). Similar observations were noted in earlier studies (Ahmed, 2011; Mohanna Rao, 2015; Chhibber *et al*., 2017).

Vomiting and anorexia are common symptoms in dogs in the later stages of renal dysfunction and can result in decreased caloric intake. Causes of vomiting and anorexia include effects of uremic toxins on the medullary emetic chemoreceptor trigger zone and gastroenteritis secondary to uremia (Washabau and Elic, 1995 and Grauer, 2007). Many medications including antibiotics, antifungals and analgesics may also produce anorexia. Prominent weight loss and weakness was observed in 68.18% and 68.18% respectively in the present study. Weight loss and weakness might result from a combination of inadequate calorie intake, the catabolic effects of uremia and intestinal mal-absorption secondary to uremic gastro-enteritis (Rubin, 1997). Weakness may be the consequence of dehydration, prolonged anorexia or hypokalemia (Kralova *et al*., 2009). Pale mucous membrane (50%) was a consistent finding and is often a characteristic of advanced stage of renal dysfunction in dogs mainly due to the presence of anemia. A major factor related to anemia in the present study appeared to be decreased erythropoietin produced by dysfunctional kidneys (Eschbach and Adamson, 1991) and hemolysis and blood loss (King *et al*., 1992). Polyuria (47.72 %) and polydipsia (47.72 %) and anuria (6.81%) was also a notable finding in the present study. Water consumption and urine production are controlled by complex interactions between plasma osmolality, fluid volume in the vascular compartment, the thirst centre, the kidneys, the pituitary gland and hypothyroidism. Increase in the renal blood flow reduces renal medullary concentrations leading to impaired water re-absorption from the distal nephron. Infection and inflammation of renal pelvis may adversely affect the counter current mechanism in renal medulla. This results in isosthenuria, polyuria, secondary polydipsia and eventually renal failure (Feldman, 2010).

Lethargy and recumbency in dogs with renal dysfunction may be due to the accumulation of nitrogenous substances in the blood, dehydration and electrolyte disturbances and this can lead to the uremic encephalopathy as indicated by Scini *et al*. (2010). Dogs with renal failure may have weakness associated with renal secondary hypothyroidism due to hypocalcemia or lactation causing increased excitability in both central nervous system and muscles which cause a peripheral neuropathy or myopathy (Raylander, 2010). Further studies are needed to establish exact patho-physiological mechanism of these changes in canine renal disorders.

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Oral ulcers and halitosis observed may have occurred as a result of gastritis and vomiting or the effect of uremic toxins on mucosal membranes which often result in anorexia (Robinson *et al.*, 1989; Grauer, 2007; and McGrotty, 2008).

Haemato-Biochemical Study

Haematology revealed a highly significant (P≤0.01) reduction in haemoglobin (9.29±0.6g/dL), PCV (28.10±1.95%) and TEC (4.84±0.34 10^6/ µL) in dogs with renal dysfunction leading to anemia when compared to control dogs (Table 1).The causes of anemia in chronic kidney diseases attributed to reduced renal production of erythropoietin, reduced red blood cell survival, gastrointestinal bleeding and uremic inhibitors of erythropoiesis, bone marrow fibrosis and nutritional deficiencies (Cowgill *et al*., 1998).

Table 1: Haemato-biochemical values of healthy control dogs and dogs with renal dysfunction (Mean±SE)

Parameters / Normal Range	Healthy Control (n=10)	Dogs with Renal Dysfunction (n=44)
Hb (g/dL)	12.46±0.49	9.29±0.65**
	(9.7 – 14)	(3.4 – 16.5)
PCV (%)	42.02± 1.39	28.10±1.95**
	(30.4 – 41.7)	(10.9 – 49.4)
TEC (10^6/µL)	6.51± 0.14	4.84± 0.34**(non-significant from normal range?)
	(5.98 – 7.27)	(1.72 – 8.2)
TLC (10^3/µL)	12.21±0.88	15.81±2.20^{NS}
	(8.93 – 17.37)	(5.04 – 56.12)
Protein (g/dL)	6.32±0.29	4.58±0.33*
	(5.2 – 7.5)	(4 – 10)
Albumin (g/dL)	2.84±0.15	2.17±0.10^{NS}
	(2.2 - 3.5)	(1.9- 3.9)
BUN (mg/dL)	20.60 ± 1.67	104.7±17.67**
	(14.5 – 28)	(32 – 430.7)
Creatinine (mg/dL)	0.80±0.08	4.22 ± 0.49**
	(0.4 – 1.1)	(2 – 12)
Sodium (mEq/L)	146.50±0.86	157.90±8.92^{NS}
	(143 – 150)	(109 – 333)
Potassium (mEq/L)	4.12 ± 0.12	4.96 ± 0.28^{NS}
	(3.7 – 4.8)	(3.8 – 10)
Phosphorus (mg/dL)	3.80±0.19	7.78±0.57**
	(2.8 – 4.5)	(3.5 – 16)
Calcium (mg/dL)	9.85±0.12	8.86±0.14^{NS}
	(9.2 – 10.2)	(7.9- 11.2)
Glucose (mg/dL)	88.70±1.88	92.67±2.60^{NS}
	(81 – 98)	(60 – 120)

*** Statistically highly significant (P≤0.01) *statistically significant (P≤0.05) NS– non significant*

Serum biochemistry revealed significant hypoproteinemia (4.58±0.33 g/dL) and mild hypoalbuminemia (2.17±0.10 g/dL), a highly significant (P≤0.01) increase in the levels of BUN (104.7±17.67 mg/dL) and

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creatinine (4.22±0.49 mg/dL) and significant hyperphosphatemia (7.78±0.57 mg/dL) as shown in Table 1. Similar observations were also reported by Bradea *et al.* (2013); Mishra *et al*. (2014); Mohana Rao (2015) and Chhibber *et al*. (2017) in chronic kidney diseases in canines. Hypoproteinemia and hypoalbuminemia in dogs with renal dysfunction could be due to the loss of protein in case of renal insufficiency (Devaux *et al.*, 1996). It may also be attributed to increased filtration of albumin through glomeruli, owing to its molecular size (Shaw and Ihle, 2013). The increased blood levels of BUN and creatinine in renal dysfunction could be due to retention of nitrogenous substances normally excreted by healthy kidneys (Cowgill *et al*., 1998 and Polzin *et al*., 2000). Serum creatinine concentration also increases as a result of the progression of kidney disease and decline of glomerular filtration rate (GFR) (Finco, 1976 and Dibartola *et al*., 1983).The increase in sodium and phosphorus values in this study could be due to the declining GFR in dogs with renal dysfunction which leads to sodium and phosphorus retention and ultimately resulting into mild hypernatremia and hyperphosphatemia (Cowgill *et al*., 1998).

Urinalysis and Urine Biochemistry in Renal Dysfunction in Dogs

One of the most significant alterations associated with renal dysfunction is the change in the urine constituent of the renal patient. Proteinuria and reduced excretory capacity are the cardinal features of renal dysfunction. Proteinuria is considered the most common marker of kidney damage.

Table 2: Urine biochemistry in renal dysfunction (Mean±SE)

Parameters / **Normal range**	**Healthy Control (n=10)**	**Dogs with Renal Dysfunction (n= 44)**
Protein (g/dL)	5.00±1.67	154.70±32.34**
	(0 – 10)	(30 – 500)
Creatinine (mg/dL)	201.50±39.88	63.60±11.40**
	(100 – 400)	(20 – 250)
Urine protein creatinine Ratio (UPC) (g/g)	0.03±0.01	2.25±0.16**
	(0 – 0.1)	(0.75 – 4.2)

***(P ≤ 0.01); Values in bracket indicates the range*

In the present study, a highly significant (P≤0.01) increase in urine protein and urine protein and creatinine ratio (UP/C) and a highly significant decrease in urine creatinine level (Table 2) was observed in comparison to healthy control dogs which is in agreement with earlier observations (Mrudula *et al*., 2005; Yathiraj, 2006; Shilpa and Yathiraj , 2006; Mohanna Rao, 2015). Proteinuria and increased UPC in renal dysfunction could be due to the glomerular damage (Polzin *et al.*, 2000).

Proteinuria is consequence of two mechanisms: the abnormal trans glomerular passage of proteins due to increased permeability of glomerular capillary wall and their subsequent impaired reabsorption by the epithelial cells of the proximal tubuli (D'Amico and Bazzi, 2002). Recent studies suggest that in dogs as in humans, persistent protienuria is associated with greater frequency of renal morbidity, renal mortality and

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mortality of all causes (Jacob *et al*., 2005). The value of proteinuria as a marker of clinically important events in the kidney arises because it can occur and subsequently vary in magnitude because of altered vascular permeability of glomerular capillary walls (possibly marking the presence of immune complexes, vascular inflammation, or intra-glomerular hypertension) or impaired tubular handling of filtered proteins (possibly marking the presence of tubulointerstitial dysfunction) or both. (Lees *et al*., 2005). In the present study it was also observed that there was persistent proteinuria with UPC values of (2.25± 0.16). This condition is often seen in dogs due to glomerular disease (stage III) (Center *et al*.,1985). In dogs with renal failure, having a UPC value ≥ 1.0 at initial evaluation is associated with increased risk of uremic morbidity and mortality (Jacob *et al*., 2005).

Conclusion

In the present study the prominent clinical signs observed were anorexia, weight loss, weakness, vomiting, emaciation, pale mucous membrane, polyuria, polydipsia, inappetence, recumbency, anuria, halitosis, oral ulcers, epistaxis, seizure, and cataract/blindness. Haemato-biochemical investigation revealed severe anemia (low Hb, PCV and TEC), proteinuria and elevated serum creatinine in dogs suffering from renal dysfunction.

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