RESEARCH ARTICLE

Early Identification of Renal Disease in Dogs with Suspected Renal Insult using Haemato-Biochemical, Urinary, and Advanced Biomarker Profiling

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Abstract

Renal disease represents a common and clinically important disorder in dogs, often associated with significant morbidity and mortality. Early renal insult frequently remains undetected when diagnosis relies solely on conventional markers such as serum creatinine, which may not increase until substantial nephron loss has occurred. Consequently, early identification of renal dysfunction is essential to enable timely therapeutic intervention, slow disease progression, and improve clinical outcomes. The present study was undertaken to assess the diagnostic value of an integrated approach combining haemato-biochemical parameters, urinary indices, and advanced renal biomarker profiling for the early identification and characterization of renal disease in dogs with suspected renal insult. Twenty-five middle-aged to geriatric dogs presenting with clinical conditions known to predispose renal injury were enrolled. Dogs suffering from gastrointestinal, urinary, hepatic and miscellaneous systemic disorders demonstrated varying degrees of renal involvement during the monitoring period. Clinical examination, haemato-biochemical profiling, urinalysis, urine protein to creatinine ratio (UPC), urine microalbumin and serum symmetric dimethylarginine (SDMA) were evaluated on day 1 and subsequently monitored on days 45 and 90. A mild elevation in urine microalbumin and symmetric dimethylarginine (SDMA) concentrations was detected in a subset of dogs upon successive evaluation on days 45 and 90. The findings demonstrated that combined assessment of haemato-biochemical parameters, urinary indices, and advanced biomarkers provides a sensitive and comprehensive approach for early identification of renal disease in dogs with suspected renal insult. Incorporation of advanced biomarker profiling alongside conventional diagnostics can facilitate earlier diagnosis, guide clinical decision-making, and potentially improve renal outcomes in canine patients.

Key words: Dogs, Renal insufficiency, Early renal biomarkers, Proteinuria, SDMA,

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Introduction

The kidneys are essential for maintaining physiological homeostasis through excretion of metabolic waste, regulation of blood pressure and acid–base balance, and support of erythropoiesis (Cotran *et al.,* 1999). Consequently, renal dysfunction produces systemic effects, leading to multisystem involvement and reduced quality of life. Renal failure is among the most common and fatal diseases in dogs, with a reported prevalence of 2-5% and ranking as the third leading cause of canine mortality (Lund *et al.*, 1999); an annual hospital prevalence of 4.94% has also been documented (Supriya, 2019). Acute renal failure commonly presents with anorexia, dehydration, depression, vomiting, diarrhea, oliguria, and painful enlarged kidneys (Aiello and Moses, 2016), whereas chronic kidney disease (CKD) involves persistent renal structural or functional alterations for more than three months. Even mild to moderate azotemia may reflect substantial nephron loss, masked by compensatory hypertrophy of remaining nephrons in early disease stages (Finco *et al.*, 1999).

Conventional biomarkers such as serum creatinine and blood urea nitrogen increase only after approximately 70-75% loss of functional nephron mass, limiting their utility for early diagnosis. The urine protein-to-creatinine ratio (UPCR) is valuable for identifying progressive renal disease and guiding therapeutic decisions (Jacob *et al.*, 2005), while combined serum and urinary biomarker assessment improves evaluation of disease severity and progression (Cobrin *et al.*, 2013). Despite these advances, early detection of renal impairment remains challenging. Novel urinary biomarkers

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offer promise for improved diagnosis by differentiating glomerular and tubular injury, thereby refining disease staging and grading (De Loor *et al.*, 2013). Against this background, the present study aimed to characterize early renal disease in dogs with suspected renal insult and normal serum creatinine through longitudinal evaluation of clinical findings, haemato-biochemical parameters, urinalysis, and emerging renal biomarkers like urine protein to creatinine ratio, urine microalbumin and serum symmetric dimethylarginine (SDMA).

Materials and Methods

The study was conducted at the Department of Veterinary Medicine and the Multi-Speciality Veterinary Hospital, Teaching Veterinary Clinical Complex, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, India on dogs presented with clinical conditions known to predispose renal injury.

Selection of Animals and Experimental Design

Twenty-five client-owned dogs aged four years and above with clinical signs suggestive of systemic illness and potential renal insult but having serum creatinine concentrations below 1.4 mg/dL were randomly selected. Dogs were categorized as mature (4-7 years, n=14), senior (8-10 years, n=7) and geriatric (>10 years n=4). Dogs suspected for renal insult on the basis of history and/or clinical signs, *viz.* dehydration, vomiting, diarrhea, inappetence, fever, anorexia, urinary incontinence, weight loss, lethargy and having serum creatinine concentrations below 1.4 mg/dL. The selected dogs on day 1 were subjected to clinical and haemato-biochemical examination including physical assessment, routine urinalysis and estimation of urine protein to creatinine ratio (UPC), blood urea nitrogen and urine microalbumin. The dogs were monitored for three months and renal biochemical examinations (BUN, creatinine, UPC, urine microalbumin), SDMA and urinalysis were performed on day 45 and 90 of the study.

Client Information and Signalment

Owner details were recorded in the clinical case records along with patient information including breed, sex, age, and body weight. A detailed clinical history was obtained from owners covering diet, water intake, urination patterns, weight changes, vaccination and deworming status, vomiting, fever, tick infestation, urinary abnormalities, possible toxin exposure, onset of clinical signs, and any previous illnesses or treatments.

Physical Examination

All dogs underwent a detailed physical examination, including recording of rectal temperature, heart rate, and respiration rate; auscultation of the heart and lungs; examination of the oral cavity, skin, hydration status, abdomen, and regional lymph nodes. Based on clinical findings, a preliminary diagnosis was made and cases were categorized as gastroenteritis (n=8), urinary disorders (n=4), hepatic disorders (n=4), or miscellaneous disorders (n=9; pyometra, inappetence, TVT, chronic weight loss, diabetes mellitus, and maxillary swelling).

Haemato-Biochemical Analysis

Approximately 2 mL of blood was collected in Na_2EDTA vials for complete blood count, and 5 mL was collected in plain vials for serum separation and biochemical analysis. Haematological parameters were measured using an automated haematology analyser (ADVIA® 2120), with differential leukocyte counts performed on Leishman's-stained blood smears. Biochemical parameters, including BUN, creatinine, ALT, ALKP, total protein, and albumin, were estimated using the Virtos DT 350 Chemistry System, while serum SDMA was measured using a commercial ELISA kit.

Urine Analysis

Urine samples from the dogs were collected in sterile plastic containers either by cystocentesis or catheterization for routine examination, *viz.* physical, chemical (by using Multistix® 10 SG Reagent Strips), and microscopic (under low & high magnification). Urine protein and urine creatinine were also estimated using Virtos DT 350 Chemistry system, and its ratio was worked out. Urine microalbumin concentrations were assessed using the Pyrogallol red method, employing a micro-protein kit.

Results and Discussion

Dogs included in the study belonged to mature, senior and geriatric age groups. A greater tendency for renal biomarker alterations was observed in senior and geriatric dogs, suggesting increased susceptibility of aging kidneys to systemic insults. The predominance of renal alterations in older dogs observed in this study has been documented in epidemiological studies conducted in dogs in India (Supriya, 2019).

Clinical Disorders Associated with Renal Insult

Dogs were presented with a variety of systemic disorders known to predispose renal injury, including gastrointestinal, urinary and hepatic conditions. Systemic illnesses may contribute to renal insult through dehydration, renal hypoperfusion, inflammatory mediators and immune-mediated mechanisms. Similar associations between extra-renal diseases and renal dysfunction have been previously described (Nenov *et al*., 2000; Jacob *et al*., 2005).

Gastro-enteritis (Group I)

The vital parameters and haemato-biochemical profile of the dogs suffering from Gastritis/Enteritis/Gastro-enteritis, *i.e.,* Group I (n=8) are presented in Table 1 and 2. On the day of presentation, the physiological parameters were within the normal reference ranges. The gastroenteritis appeared to have insignificant impact on the heart rate and respiration rate. However, in 37.5% of the cases, the rectal temperature was elevated and in 12.5% of the cases, it was lower than the reference range. In cases of gastroenteritis, laboratory testing may be required to rule out extra-gastrointestinal conditions such as acute kidney injury, hepatitis, and pancreatitis, and to identify associated electrolyte and acid-base imbalances contributing to clinical signs (Lawrence and Lidbury, 2015). Haemato-biochemical analysis showed anaemia (low Hb and PCV) in 25% of cases (n=2), likely due to gastrointestinal blood loss. Similar reductions in haemoglobin, TEC, and PCV have been reported in dogs with gastroenteritis (Lee *et al.*, 2012; Ali *et al.*, 2014). Elevated TLC and absolute neutrophil counts in 12.5% and 37.5% of dogs, respectively, suggest an infectious etiology. Increased serum ALT and ALKP and decreased albumin were each observed in 25% of cases (n=2), consistent with earlier findings (Arora *et al.*, 2018). Hypoalbuminemia and elevated AST may reflect hepatic involvement and severe protein-losing enteropathy (Grigonis *et al.*, 2002).

Serum and urinary renal biomarkers, including BUN, serum creatinine, SDMA, urinary microalbumin, urine protein-creatinine ratio, urine pH, and urine specific gravity, were monitored for three months (Table 2). No significant changes were observed, indicating absence of renal injury in dogs with gastritis/enteritis/gastroenteritis. Similar findings were reported by Arora *et al.* (2018), who noted no differences in BUN and creatinine between dogs with gastroenteritis and healthy controls. In contrast, Qurollo *et al.* (2019) documented frequent renal failure in dogs with ehrlichiosis, characterized by azotemia and increased SDMA, ALT, and ALP. Serum SDMA has been shown to correlate strongly with serum creatinine and GFR in dogs with renal failure (Nabity *et al.*, 2015).

Urinary tract disorders (Group II)

The vital parameters, haemato-biochemical profile, and renal injury biomarkers of dogs with urinary disorders (Group II, n=4) are presented in Tables 1 and 2. At presentation, rectal temperature, heart rate, and respiration rate were within normal limits, and haematological evaluation revealed normal Hb and PCV values. However, TLC and absolute neutrophil counts were elevated in cases of cystitis, likely reflecting a bacterial etiology. Serum biochemical parameters remained within normal reference ranges. In contrast, Roopali *et al.* (2018) reported decreased Hb, PCV, TEC, and lymphocyte counts, with significantly increased TLC and neutrophils,

Table 1: Vital parameters and haemato-biochemical profile in dogs suffering from gastro-enteritis and urinary tract, hepatic and miscellaneuos disorders

Parameter	Reference range*	Gastro-enteritis	Urinary tract disorders	Hepatic disorders	Miscellaneous diseases
		Mean ± SE (n=8)	Mean ± SE (n=4)	Mean ± SE (n=4)	Mean ± SE (n=9)
Rectal temperature (^{o}F)	101-103	102.20 ± 0.70	102.10 ± 0.20	101.95 ± 0.70	102.42 ± 0.56
Heart rate (beat/min)	70 - 120	114.00 ± 4.60	101.50 ± 6.30	133.00 ± 20.80	129.00 ± 7.40
Respiration rate (breath/min)	16 - 34	30.75 ± 0.90	32.75 ± 4.40	28.00 ± 2.40	34.33 ± 2.10
Hb (g/dL)	12 - 18	13.20 ± 0.90	14.05 ± 0.80	12.75 ± 2.70	13.76 ± 0.90
PCV (%)	37 - 55	37.65 ± 2.40	39.25 ± 2.00	34.40 ± 6.40	38.57 ± 2.10
TLC (/cmm)	6000-17000	12075.00±1681.70	19725.00±4770.20	22175.00 ± 3751.00	17191.11 ± 3614.50
Absolute neutrophil count (/cmm)	3000-11500	10305.25 ± 1640.10	16852.00 3992.50	19302.00±3330.60	14906.22 ± 3673.90
Absolute lymphocyte count (/cmm)	1000-4800	1527.00 ± 298.60	2329.00 ± 1042.10	2238.50 ± 439.30	2057.33 ± 334.70
Absolute eosinophil count (/cmm)	0 - 1300	346.250 ± 202.40	544.00 ± 474.70	634.50 ± 301.10	227.55 ± 106.70
Platelets (/cmm)	200000-800000	242375.00±29694.80	399500±129162.30	287250.00±92061.90	264555.50±67134.60
Serum ALT (U/L)	8.2 - 57	39.25 ± 7.90	37.25 ± 7.00	277.75 ±158.50	46.33 ± 11.70
Serum ALKP (U/L)	10.6- 101	116.00 ± 40.00	142.75 ± 77.00	686.25 ± 352.70	283.66 ± 146.60
Serum total proteins (g/dL)	5.5 - 7.5	5.80 ± 0.40	6.37 ± 0.20	5.60 ± 1.10	5.97 ± 0.30
Serum albumin (g/dL)	2.6 - 4.0	2.68 ± 0.20	3.55 ± 0.10	1.92 ± 0.30	2.96 ± 0.10
Serum globulin (g/dL)	2.7 - 4.4	3.11 ± 0.20	2.82 ± 0.20	3.67 ± 0.90	3.01 ± 0.20
Blood glucose (mg/dL)	80 - 120	112.00 ± 6.50	106.25 ± 3.90	90.00 ± 11.50	103.20 ± 7.60

*Textbook of Small Animal Practice. Saunders, 3rd edition (2006) along with mild azotemia and reduced serum proteins in animals with urinary tract infections.

Renal injury biomarkers showed no significant alterations during the study period, except transient elevations in urine microalbumin and urine pH in one dog at presentation and increased UPCR (urine protein to creatinine ratio) in one dog on day 45, all of which normalized on subsequent evaluations. Hall *et al*. (2016) demonstrated that serum SDMA enables early detection of renal failure, with elevated levels observed in 17 of 19 affected dogs. Borderline proteinuric dogs should be re-evaluated within two months using UPC, as persistent proteinuria is associated with poor prognosis and reduced survival time (Elliott and Watson, 2009).

Hepatic disorders (Group III)

The vital parameters, haemato-biochemical profile, and renal injury biomarkers of dogs with hepatic disorders (Group III, n=4) are presented in Tables 3 and 4. On day 1, tachycardia was observed in 75% of dogs. Reduced Hb and PCV were noted in 50% of cases (n = 2), while TLC and absolute neutrophil counts were elevated in 75% and 100% of cases, respectively. These alterations were associated with an infectious etiology, confirmed by microscopic detection of bacteria in peritoneal fluid.

Thrombocytopenia was recorded in 25% of cases (n=1). Serum ALT and ALKP were increased in all dogs, and those with ascites and hepatitis showed decreased serum total protein and albumin levels. Similar findings, including anaemia, reduced PCV, leucocytosis, neutrophilia, and thrombocytopenia, have been reported in canine hepatic disorders (Prebavathy *et al*., 2020). Elevated hepatic enzymes likely reflect hepatocellular membrane damage, necrosis, and inflammation, with the magnitude of increase proportional to the extent of hepatocyte injury (Kramer and Hoffman, 1997). Thrombocytopenia in liver disease may result from splenic sequestration, reduced thrombopoietin synthesis, immune-mediated platelet destruction, and increased consumption due to low-grade disseminated intravascular coagulopathy (Prins *et al*., 2010).

Renal biomarker analysis showed that BUN and serum creatinine remained within normal reference ranges throughout the study period. In contrast, Elhiblu *et al*. (2015) reported increased BUN and creatinine in dogs with hepatic disease, and Sampaio *et al*. (2014) identified renal dysfunction as a common complication of end-stage liver disease. Mean SDMA values were within normal limits; however, one dog with ascites exhibited persistently elevated SDMA on days 1, 45, and 90. In this dog, urine microalbumin (48.33, 56.10, and 36.54 mg/dL on days 1, 45, and 90, respectively) and urine protein–creatinine ratio were also increased. SDMA serves as a reliable marker of glomerular filtration rate, as it is predominantly eliminated via renal filtration (Brown, 2014).

Miscellaneous diseases (Group IV)

The vital parameters, haemato-biochemical profile, and renal injury biomarkers of dogs with conditions associated with

Table 2: Renal insult biomarkers in dogs suffering from gastro-enteritis and urinary tract disorders associated with possible renal insult (Mean ± SE)

Renal Biomarker	Reference range*	Gastro-enteritis (n=8)			Urinary tract disorders (n=4)		
		Day 1	Day 45	Day 90	Day 1	Day 45	Day 90
BUN (mg/dL)	8 – 28	$14.75^a \pm 1.90$	$15.0^a \pm 2.10$	$14.75^a \pm 1.20$	$10.50^a \pm 1.60$	$14.75^a \pm 2.10$	$15.25^a \pm 3.90$
Serum creatinine (mg/dL)	0.5 – 1.4	$0.73^a \pm 0.09$	$0.75^a \pm 0.06$	$0.73^a \pm 0.07$	$0.72^a \pm 0.10$	$0.82^a \pm 0.07$	$0.82^a \pm 0.10$
SDMA (µg/dL)	<18	$4.22^a \pm 1.20$	$3.40^a \pm 0.70$	$3.54^a \pm 0.70$	$4.97^a \pm 2.70$	$4.80^a \pm 2.00$	$5.73^a \pm 3.10$
Urine microalbumin (mg/dL)	1 – 35	$31.17^a \pm 3.10$	$26.48^a \pm 2.00$	$24.88^a \pm 1.57$	$33.71^a \pm 5.30$	$28.28^a \pm 2.90$	$25.40^a \pm 2.10$
UPCR	Note**	$0.08^a \pm 0.02$	$0.12^a \pm 0.04$	$0.11^a \pm 0.01$	$0.09^a \pm 0.03$	$0.14^a \pm 0.04$	$0.08^a \pm 0.01$
Urine pH	5.5 – 7.5	$6.12^a \pm 0.10$	$6.12^a \pm 0.10$	$6.3^a \pm 0.10$	$7.37^a \pm 0.30$	$6.97^a \pm 0.30$	$6.95^a \pm 0.05$
Urine specific gravity	1.015 – 1.060	$1.028^a \pm 0.001$	$1.026^a \pm 0.001$	$1.025^a \pm 0.001$	$1.022^a \pm 0.002$	$1.022^a \pm 0.001$	$1.018^a \pm 0.001$

*Note: UPCR <0.2 nonproteinuric; 0.2-0.5 borderline, and >0.5 proteinuric. Figures with different superscripts differ significantly (p≤0.05). *Source: Textbook of Small Animal Practice Saunders 3rd edition (2006).

Table 3: Renal insult biomarkers in dogs suffering from Hepatic disorders and miscellaneous disease conditions associated with possible renal insult (Mean ± SE)

Renal Biomarker	Reference range*	Hepatic disorders (n=4)			Miscellaneous diseases (n=9)		
		Day 1	Day 45	Day 90	Day 1	Day 45	Day 90
BUN (mg/dL)	8 – 28	12.75^{a}± 2.86	15.00^{a}± 5.35	14.50^{a}± 2.46	10.11^{a}± 0.90	15.77^{a}± 2.40	15.00^{a}± 1.90
Serum creatinine (mg/dL)	0.5 – 1.4	1.02^{a}±0.16	1.05^{a}± 0.06	0.85^{a}± 0.02	0.80^{a}± 0.08	0.90^{a}± 0.09	0.80^{a}± 0.04
SDMA (µg/dL)	<18	11.09^{a}± 6.47	8.11^{a}± 6.87	7.93^{a}± 6.13	4.64^{a}± 1.52	4.28^{a}± 1.35	5.11^{a}± 1.61
Urine microalbumin (mg/dL)	1 – 35	46.90^{a}± 13.00	37.64^{a}± 6.50	27.65^{a}± 4.31	34.68^{a}± 3.5	31.06^{a}± 2.54	26.50^{a}± 2.1
UPCR	Note**	0.30^{a}± 0.12	0.10^{a}± 0.03	0.10^{a}± 0.06	0.09^{a}± 0.02	0.11^{a}± 0.02	0.10^{a}± 0.01
Urine pH	5.5 – 7.5	6.37^{a} ± 0.20	6.27^{a} ± 0.10	6.22^{a} ± 0.20	6.27^{a} ± 0.20	6.25^{a} ± 0.10	6.47^{a} ± 0.10
Urine specific gravity	1.015 – 1.060	1.024^{a} ± 0.003	1.023^{a} ± 0.001	1.024^{a} ± 0.001	1.019^{a} ± 0.001	1.019^{a} ± 0.001	1.020^{a} ± 0.001

**Note: UPCR <0.2 nonproteinuric; 0.2-0.5 borderline, and >0.5 proteinuric. Figures with different superscripts differ significantly ($p \leq 0.05$). *Source: Textbook of Small Animal Practice Saunders 3rd edition (2006).

possible renal insult (Group IV, n=9), including pyometra, diabetes mellitus, chronic weight loss, transmissible venereal tumor, maxillary swelling, and pyrexia of unknown origin, are presented in Tables 3 and 4. At presentation, 33.3% of dogs had pyrexia, mainly in cases of pyrexia of unknown origin and transmissible venereal tumour. Elevated heart and respiration rates were observed in 44.4% and 66.6% of dogs, respectively. Marginal reductions in Hb (22.2%) and PCV (44.4%) were noted, while increased TLC and absolute neutrophil counts were seen in 33.3% of cases. Thrombocytopenia was common (55.5%), particularly in dogs with pyrexia of unknown origin, pyometra, and diabetes mellitus. Serum ALT and ALKP were elevated in 44.4% and 55.5% of cases, respectively, likely reflecting toxaemic injury and hepatic hypoxia (Shah *et al.*, 2013).

Serum and urinary renal biomarkers, including BUN, creatinine, SDMA, urinary microalbumin, UPCR, urine pH, and urine specific gravity, showed no significant alterations during the three-month monitoring period, indicating absence of overt renal injury. Dogs aged 4-7 years are considered mature, while senior (8-10 years) and geriatric (>10 years) dogs progressively exhibit age-related physiological and health changes, necessitating closer clinical monitoring and tailored management.

Conclusion

The study establishes that reliance on serum creatinine alone is inadequate for early detection of renal disease in dogs. Incorporation of serum SDMA, UPC and urine microalbumin enables identification of renal dysfunction at a subclinical stage. Routine screening of these biomarkers in dogs with systemic illness and advancing age is strongly recommended to facilitate early therapeutic intervention and improve long-term renal outcomes.

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