International Journal of Veterinary Sciences and Animal Husbandry

ISSN: 2456-2912
NAAS Rating (2025): 4.61
VET

www.veterinarypaper.com
Received: 12-06-2025
Accepted: 14-07-2025

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Correlative analysis of UACR with conventional renal biomarkers in the early diagnosis of renal dysfunction

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DOI: https://www.doi.org/10.22271/veterinary.2025.v10.i9e.2570

Abstract
The present study evaluated the diagnostic potential of urine albumin-to-creatinine ratio (UACR) in detecting renal dysfunction in dogs and its correlation with conventional biomarkers. Thirty-seven dogs were enrolled, including six healthy controls, six acute kidney injury (AKI) cases, and 25 dogs with chronic kidney disease (CKD) staged as per IRIS guidelines. Serum creatinine and blood urea nitrogen (BUN) levels were significantly elevated in AKI and CKD dogs compared to controls, indicating progressive azotaemia. UACR values were markedly increased across all CKD stages and in AKI, showing a strong correlation with conventional renal biomarkers. Notably, UACR levels rose progressively with advancing CKD stages, highlighting its utility in disease staging and monitoring. The findings demonstrate that UACR is a sensitive and non-invasive biomarker for early diagnosis and progression assessment of canine renal dysfunction, supporting its integration into clinical practice.

Keywords: UACR, renal dysfunction, chronic kidney disease, acute kidney injury, biomarkers, dogs

1. Introduction
Renal dysfunction means structural or functional damage in one or both kidneys [6]. AKI is typically marked by a sudden decline in glomerular filtration rate (GFR), reduced urine output and impaired renal solute excretion [3]. In contrast, CKD is characterized by long-standing functional or structural abnormalities in one or both kidneys, usually persisting for two months or more. Both conditions can coexist in the same patient, a situation referred to as acute on chronic kidney disease. Generally, CKD is considered irreversible and progressive, while AKI may be reversible with timely intervention [16]. In canine veterinary medicine, chronic kidney disease (CKD) is staged following the International Renal Interest Society (IRIS) criteria, which incorporate sub-staging parameters such as systemic blood pressure and urinary protein levels to assess disease severity and predict clinical outcomes [2, 16]. Diagnostic frameworks for acute kidney injury (AKI) and chronic kidney disease (CKD) are instrumental in recognizing instances of renal damage that may be amenable to therapeutic intervention. Nonetheless, accurate classification of the injury type and underlying pathology remains a critical first step for the veterinarian [5]. Blood urea nitrogen (BUN) and serum creatinine are principal metabolic byproducts routinely eliminated by the kidneys. When renal function is compromised, these substances accumulate in the bloodstream, making their elevated concentrations reliable biochemical markers for detecting kidney dysfunction [10]. At 75-90% loss of nephron functioning, the waste starts building up in the blood, causing symptoms like poor appetite, weight loss, lethargy, vomiting, and diarrhoea [17, 19]. On the other hand, identifying reliable early CKD biomarkers remains a challenge.
Several studies have highlighted albuminuria as a potential early marker of renal pathology [7, 24]. Notably, the urine albumin-to-creatinine ratio (UAC) has been shown to be markedly elevated in dogs diagnosed with chronic kidney disease (CKD) relative to clinically healthy counterparts [1]. The study demonstrated significant elevation of ACR in dogs with renal dysfunction and proposed UACR >64.20 mg/g as a diagnostic threshold [11]. Albuminuria may arise secondary to a range of systemic conditions, including inflammatory, infectious metabolic,

neoplastic, and cardiovascular disorders [1, 7, 8, 18].
This investigation evaluated the diagnostic potential of the urine albumin-to-creatinine ratio (UAC) for early detection of chronic kidney disease (CKD) in dogs, and explored its correlation with established renal biomarkers including blood urea nitrogen (BUN) and serum creatinine (CREA).

2. Materials and Methods
The present study was carried out in the Veterinary College Hospital, Department of Veterinary Medicine, Veterinary College, Hebbal, Bengaluru, KVAFSU University Bidar.

2.1 Animals for the study
2.1.1 Apparently healthy (control) dogs
Six apparently healthy dogs irrespective of breed and gender with age more than 6 years brought to the Veterinary College Hospital, Hebbal, Bengaluru for regular health examination were considered as the control group. Animal with any medication was not included.

2.1.2 Clinical cases (Study group)
Dogs aged above six years presented to the Veterinary College Hospital, Hebbal, Bengaluru with clinical signs indicative of renal dysfunction were selected as study population.

2.1.2.1 AKI Group
Dogs aged above six years presented to the Veterinary College Hospital, Hebbal, Bengaluru with history, clinical signs, laboratory findings and renal sonography changes suggestive of acute kidney injury were considered as AKI Group.

2.1.2.2 CKD Group and Staging of CKD
Dogs aged above six years presented to the Veterinary College Hospital, Hebbal, Bengaluru with history, clinical signs, laboratory findings and renal sonography changes suggestive of chronic kidney disease were considered as CKD Group.
Staging of CKD was done based on the guidelines of IRIS board as Stage I (<1.4 mg/dL), Stage II (1.4 - 2.8 mg/dL), Stage III (2.9 - 5.0 mg/dL) and Stage IV (>5.0 mg/dL). The IRIS stage of CKD was determined according to the 2019 version, based on serum creatinine concentration. To stage CKD based on serum creatinine values minimum of two serum creatinine values were taken at week apart to assess the stability of CKD.

2.2 Collection of Clinical samples
2.2.1 Serum
Two millilitres of whole blood was collected from cephalic or saphenous vein of both suspected and apparently healthy dogs in AV LaboTube serum vacutainer and allowed for stable clot formation at room temperature for 20 min, and then the samples were centrifuged at 3000 rpm for 10 min to collect the serum samples and processed the sample using semi-automatic serum biochemical analyzer RX-50 of Micro Lab for estimation of serum creatinine and blood urea nitrogen.

2.2.2 Urine
About 10 millilitres of urine were aseptically collected from both apparently healthy and clinically suspected dogs, using sterile urine collection vials preferably via catheterization to minimize contamination. The samples were subsequently analyzed for urine creatinine and albumin concentrations using the Abbott Urometer 120 urine analyzer.

2.3 Statistical Analyses
The numerical data obtained in this study from both apparently healthy dogs and the dogs with Renal dysfunction were examined using statistical techniques including Mean, Standard Deviation, Standard Error, and independent T-Test for evaluating the significance of comparison.
Formulae for UACR (mg/g) calculation used was

$$\text{UACR(mg/g)} = \frac{\text{Urine albumin (mg/dL)}}{\text{Urine creatinine (mg/dL)}} \times 1000$$

3. Results and Discussion
Study population
The study included total of 6 apparently animals and 31 dogs with Renal dysfunction. Out of 31 dogs 6 dogs were each of AKI, stage 1, stage 2 and stage 3 CKD and remaining 7 dogs were stage 4 CKD.

Estimation of renal biomarkers
Table 1 presents a comparative analysis of renal biomarkers between apparently healthy dogs (n=6) and those diagnosed with acute kidney injury (AKI) (n=6). Dogs with AKI exhibited significantly elevated serum creatinine (5.53 ± 0.96 mg/dL) and blood urea nitrogen (BUN) levels (104.58 ± 17.54 mg/dL) compared to healthy controls (0.56 ± 0.06 mg/dL and 12.25 ± 0.42 mg/dL, respectively), indicating marked azotaemia ($p<0.01$). Urinary albumin concentrations were also notably higher in the AKI group (14.02 ± 2.03 mg/dL vs. 5.48 ± 1.02 mg/dL), reflecting increased glomerular permeability. Conversely, urine creatinine levels were reduced in AKI dogs (73.55 ± 6.77 mg/dL) relative to controls (110.49 ± 9.85 mg/dL), potentially due to impaired renal filtration. The urine albumin-to-creatinine ratio (UAC) was markedly elevated in the AKI cohort (193.48 ± 26.75 mg/g), reinforcing the presence of significant proteinuria and renal dysfunction. All differences were statistically significant ($p<0.01$), underscoring the diagnostic utility of these parameters in differentiating AKI from normal renal physiology.
In the present study there was significant elevation in creatinine value in dogs with AKI compare to apparently healthy dogs. The reason for elevated creatinine in acute kidney injury (AKI) primarily reflects a sudden decline in glomerular filtration rate (GFR) due to abrupt damage to renal tubular structures [14, 21, 22].
As per the findings of the present study there was significant increase in the mean BUN value in dogs with AKI compare to apparently healthy dogs. The reason for elevated blood urea nitrogen (BUN) in dogs with acute kidney injury (AKI) primarily results from a reduced glomerular filtration rate (GFR), which impairs the kidney's ability to excrete nitrogenous waste products derived from protein metabolism [4, 21, 22].
There was significant elevation in the mean value of UACR in case of AKI compare to apparently healthy dogs. A marked increase in albumin-to-creatinine ratio (ACR) has been observed in dogs with renal dysfunction, with a proposed urinary albumin-to-creatinine ratio (UACR) threshold exceeding 64.20 mg/g serving as a potential diagnostic indicator [11]. In acute kidney injury (AKI), the urine albumin-to-creatinine ratio (UACR) may be elevated due to a

combination of glomerular and tubular dysfunction. Damage to the glomerular filtration barrier allows albumin to leak into the urine, while impaired tubular reabsorption further contributes to microalbuminuria.

Table 1: Comparative analysis of renal biomarkers between apparently healthy dogs and Dogs with AKI

Variables	Apparently healthy dogs (n=6)	Dogs with AKI (n=6)
Creatinine	0.56 ± 0.06	5.53 ± 0.96**
Blood urea nitrogen (BUN)	12.25 ± 0.42	104.58 ± 17.54**
Urine Albumin (mg/dL)	5.48 ± 1.02	14.02 ± 2.03**
Urine creatinine (mg/dL)	110.49 ± 9.85	73.55 ± 6.77**
UAC (mg/g)	48.51 ± 10.25	193.48 ± 26.75**

Note: *-significant at P< 0.05 and **- significant at P< 0.01 compare to control group

Table 2 summarizes renal biomarker profiles across apparently healthy dogs (n=6) and those diagnosed with chronic kidney disease (CKD), stratified by IRIS stages 1 through 4. A clear stage-wise escalation in serum creatinine and blood urea nitrogen (BUN) levels was observed, reflecting progressive renal impairment. Creatinine rose from 1.35 ± 0.022 mg/dL in Stage 1 to 8.1 ± 0.70 mg/dL in Stage 4, while BUN increased from 30 ± 1.31 mg/dL to 136.30 ± 26.18 mg/dL indicating worsening azotemia. Urinary albumin concentrations were significantly elevated in CKD dogs across all stages compared to healthy controls (5.48 ± 1.02 mg/dL), peaking in Stage 2 (25.8 ± 3.16 mg/dL) and gradually declining in later stages, possibly reflecting tubular exhaustion or reduced filtration capacity. Urine creatinine levels remained comparable in early stages but declined significantly in Stage 3 (78.56 ± 12.42 mg/dL) and Stage 4 (45.4 ± 9.14 mg/dL), suggesting impaired concentrating ability. The urine albumin-to-creatinine ratio (UAC) showed a consistent upward trajectory, rising from 180.33 ± 11.96 mg/g in Stage 1 to 318.56 ± 14.52 mg/g in Stage 4, underscoring progressive proteinuria and glomerular dysfunction.

There was progressive elevation in mean creatinine value as stage advances in case of CKD compared to apparently healthy dogs. The reason for progressive elevation in creatinine value may be due to declining glomerular filtration rate (GFR) due to progressive nephron loss [9, 11, 13, 14, 15, 20].

Similarly, there was progressive elevation in mean BUN value in case of CKD compared to apparently healthy group. The reason for progressive elevation in BUN value may be due to declining glomerular filtration rate (GFR) due to progressive nephron loss. However, due to its sensitivity to extrarenal influences, BUN should be used in conjunction with more specific markers [9, 11, 14, 20, 21].

The value of mean UACR were markedly elevated in all stages of CKD. The reason for elevation in urine albumin-to-creatinine ratio (UACR) observed in CKD may be attributed to concurrent glomerular and tubular impairment. Disruption of the glomerular filtration barrier permits albumin to pass into the urine, while compromised tubular reabsorptive function exacerbates albumin loss, contributing to microalbuminuria and a rise in UACR [11, 12, 20, 23].

Table 2: Comparative analysis of renal biomarkers between apparently healthy dogs and Dogs with CKD

Variables	Apparently healthy dogs (n=6)	Dogs with CKD			
		Stage 1 (n=6)	Stage 2 (n=6)	Stage 3 (n=6)	Stage 4 (n=7)
Creatinine (mg/dL)	0.56 ± 0.06	1.35±0.022**	2.38±0.217**	3.72±0.21**	8.1±0.70**
Blood urea nitrogen (BUN) (mg/dL)	12.25 ± 0.42	30±1.31**	52.71±10.66**	74.27±6.02**	136.30±26.18*
Urine Albumin (mg/dL)	5.48 ± 1.02	19.02±2.97**	25.8±3.16**	21.58±2.36**	14.21±2.54**
Urine creatinine (mg/dL)	110.49 ± 9.85	104.17±12.34	113.36±35.41	78.56±12.42**	45.4±9.14**
UAC (mg/g)	48.51 ± 10.25	180.33±11.96**	231.6±16.47**	261.35±17.54**	318.56±14.52**

Note: *-significant at P< 0.05 and **- significant at P< 0.01 compare to control group

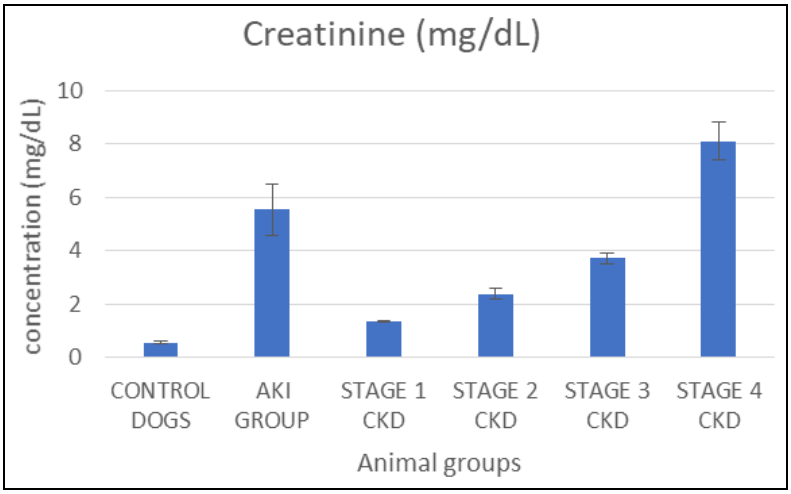

Fig 1: Creatinine (mg/dL) in dogs with Renal dysfunction

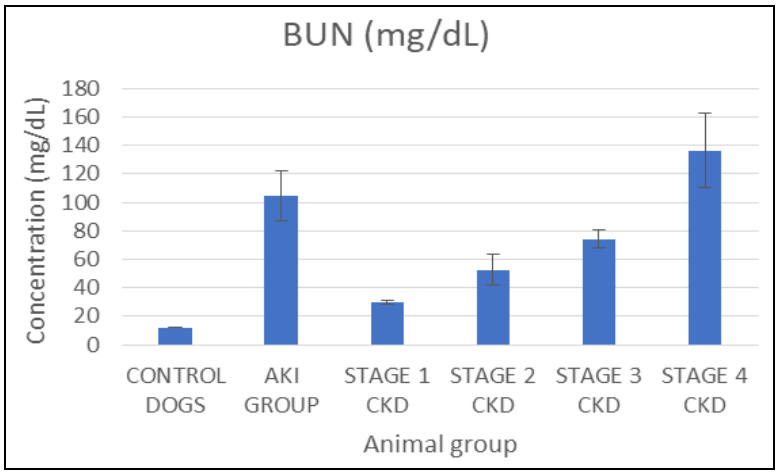

Fig 2: Blood Urea Nitrogen (mg/dL) in dogs with Renal dysfunction

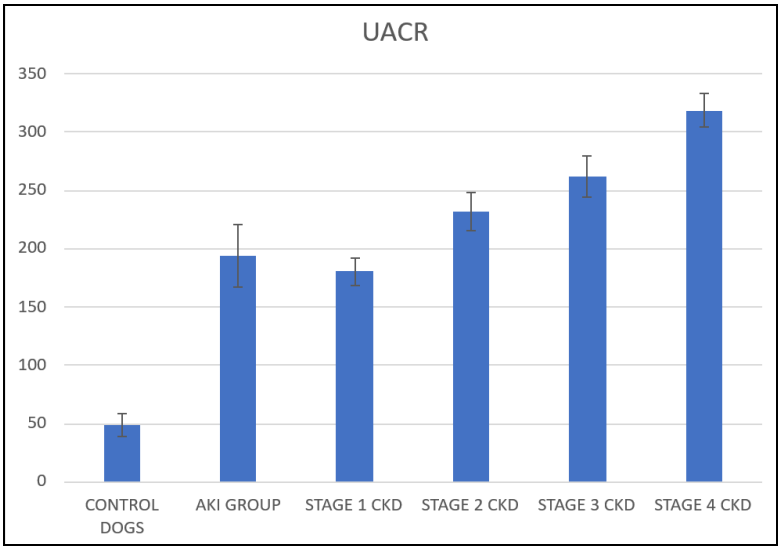

Fig 3: Urine Albumin to Creatinine ratio in dogs with Renal dysfunction

4. Conclusion

The present study underscores the diagnostic utility of the urine albumin-to-creatinine ratio (UACR) as a sensitive biomarker for identifying renal dysfunction in dogs, particularly in the early stages of chronic kidney disease (CKD). UACR values were significantly elevated across all CKD stages and in acute kidney injury (AKI), correlating well with conventional renal indicators such as serum creatinine and blood urea nitrogen (BUN). The progressive increase in UACR with advancing CKD stages highlights its potential in staging disease severity and monitoring progression. Moreover, the marked elevation of UACR in AKI cases suggests its responsiveness to acute glomerular and tubular injury. These findings support the integration of UACR into routine diagnostic panels for canine renal assessment, offering clinicians a non-invasive, quantifiable tool to enhance early detection, staging accuracy, and therapeutic decision-making in both AKI and CKD.

Conflict of Interest
Not available

Financial Support
Not available

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How to Cite This Article
Prajwal TR, Ramesh PT, Lathamani VS, Malathi V, Sharada R, Renukaradhya GJ. Correlative analysis of UACR with conventional renal biomarkers in the early diagnosis of renal dysfunction. International Journal of Veterinary Sciences and Animal Husbandry. 2025;10(9) 308-312.