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## Cystatin C as biomarkers of chronic kidney diseases in the dog

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### Abstract

Chronic kidney disease describes the gradual loss of kidney function and loss of the ability of kidneys to excrete waste products, concentrate urine, electrolytes and fluid balance leading to retention of creatinine, urea and other metabolic waste products. Routinely used biomarkers like serum creatinine and blood urea nitrogen (BUN) are not specific or sensitive in diagnosis disease. Therefore, the present study was planned to evaluate the correlation of Cystatin C with the severity of disease and with BUN & creatinine, respectively. The investigation was carried out on 24 clinical cases suspected of renal failure in dogs on the basis of clinical signs admitted at (VCC), Lala Lajpat Rai University of Veterinary and Animal Sciences (LUVAS), Hisar. All the dogs were divided into three categories based on the duration of presentation of cases after emergence of the clinical signs. Serum from affected animal and 6 apparently healthy animal was used to evaluate Cystatin C using ELISA kits whereas BUN and creatinine were calculated using biochemistry autoanalyzer. Correlation between Cystatin C with BUN and Creatinine was determined using correlation. Cystatin C were significantly elevated in dogs suffering from renal failure as compared to the control group. Among different category, in dogs showing atypical signs of renal failure significantly ( $<0.01$ ) positive correlation between cystatin C with serum creatinine & BUN. Mild illness were showed significantly ( $<0.01$ ). This can concluded that cystatin c as early diagnostic biomarker.

**Keywords:** Biomarker, chronic renal failure, cystatin C, dogs

### Introduction

Renal failure is the clinical syndrome that occurs when the kidneys are no longer able to maintain their regulatory, excretory and endocrine function which results in retention of nitrogenous solutes and derangement of fluid, electrolyte and acid base balance. Renal failure is one of the common diseases encountered in dogs and it is one of the major causes of death in young (acute renal failure) and older dogs (chronic renal failure) (Kraje, 2002) <sup>[1]</sup>. Renal failure in dogs is diagnosed on basis of structural damage to the kidneys and decreased renal function or both.

Now a day's noninvasive method of detection of disease and process of underlying disease. An ideal biomarker to detect kidney disease would be specific, able to detect both AKI and CKD, sensitive for detecting early disease, capable of documenting extent or severity of disease, monitoring disease progression, predictive of clinical outcome. Routinely used biomarkers like serum creatinine and blood urea nitrogen (BUN) are not specific or sensitive in diagnosis disease in early stages. Therefore, the present study was planned to evaluate the correlation of Cystatin C with the severity of disease and relate with the values of BUN & creatinine, respectively.

### Materials and Methods

The investigation was carried out on 24 clinical cases suspected of renal failure in dogs on the basis of clinical signs admitted at (VCC), Lala Lajpat Rai University of Veterinary and Animal Sciences (LUVAS), Hisar. All the dogs were divided into three categories based on the duration of presentation of cases after emergence of the clinical signs. Serum from affected animal and 6 apparently healthy animals was used to evaluate Cystatin C using ELISA kits whereas BUN and creatinine were calculated using a biochemistry autoanalyzer. All the dogs were divided into three categories atypical, mild (illness less than 10 days) and

severe based on the duration of presentation of cases after emergence of the clinical signs. Correlation between Cystatin C with BUN and Creatinine was determined using correlation.

### Results and Discussion

Mean value of cystatin C was remarkably increased  $4.10 \pm 1.31$  mg/l in dogs suffering from chronic renal failure as compared to the control group  $2.22 \pm 0.41$  mg/l with a statistically significant difference. Similarly finding have been observed by many researchers [Braun *et al.*, (2002); Almy *et al.*, (2002); Chacar *et al.*, (2016)]<sup>[3, 2, 4]</sup> showing an increase in cystatin C value in dogs suffering from renal failure.

Cystatin C is produced by all cells at constant rate freely filtrate by the renal glomerulus and its concentration-dependent on the glomerular rate in case of renal failure when GFR decreases, the plasma concentration of cystatin c increase and elevated level of cystatin C can be observed. Increase in value of cystatin C has been observed in present study which clearly indicates reduced GFR and malfunctioning of kidney.

Relationship between mean BUN, serum Creatinine, and Cys-C concentrations were  $19.8 \pm 13.6$  mg/dl,  $0.95 \pm 0.38$  mg/dl and  $0.33 \pm 0.15$  mg/l, respectively.; A strong correlation was found Serum creatinine, BUN with Cystatin C in Group I (Atypical group). In Group II (Mild illness) BUN with Cystatin C and in Group III Serum Creatinine, BUN with Cystatin C. Similar findings were reported by N. Iwasa *et al.* (2018)<sup>[5]</sup>, Serum Cys-C concentrations were positively correlated with and with BUN ( $r=0.685$ ), Cre  $r=0.679$  ( $p<0.01$ ). In this study, the serum Cys-C concentration showed significant positive correlations with serum BUN and Cre concentrations. The serum Cys-C concentration provided a good indication of the future risk of progression of renal diseases in the dogs. Acc. to N. Iwasa *et al.*, (2018)<sup>[5]</sup> study suggest that serum CysC concentration could be a good prognostic marker for chronic kidney diseases. The results in the present study indicate that serum Cys-C concentration may also be a promising renal prognostic marker in dogs

**Table 1:** Showing mean of cystatin C value of dogs suffering from renal failure and control

Parameter	Renal disease Mean±SE	Control
Cystatin C (mg/l)	$4.101 \pm 1.31^*$	$2.222 \pm 0.41$

**Table 2:** Correlation between serum biomarker

	BUN	Serum creatinine	Cystatin C
BUN	1	0.914*	0.886*
Serum creatinine	0.914*	1	0.877*
Cystatin C	0.886*	0.877*	1

\* Statistical correlation at ( $p<0.01$ )

**Table 3:** Correlation between different Serum biomarker

	BUN	Serum creatinine	Cystatin c
BUN	1	0.693	0.257
Serum creatinine	0.693	1	-0.18
Cystatin C	0.257	-0.18	1

\* Statistical correlation at ( $p<0.01$ )

**Table 4:** Correlation between different Serum biomarker

	BUN	Serum creatinine	Cystatin C
BUN	1	0.841**	0.188
Serum creatinine	0.841**	1	0.235
Cystatin C	0.188	0.235	1

\* Statistical correlation at ( $p<0.01$ )

\*\* Statistical correlation at ( $p<0.05$ )

### Conclusion

In conclusion, the study demonstrated a significant elevation in cystatin C levels among dogs afflicted with chronic renal failure compared to the control group, indicative of compromised renal function. This finding aligns with prior research, underlining cystatin C's utility as a marker for renal dysfunction. Furthermore, strong correlations between cystatin C and traditional biomarkers like BUN and serum creatinine were evident across different illness severities, echoing previous studies' observations. Notably, the study underscores the potential of serum cystatin C concentration as a prognostic indicator for renal diseases in canines, as supported by similar research. Thus, the results suggest that monitoring cystatin C levels could offer valuable insights into the prognosis of renal conditions in dogs, aiding in early intervention and management strategies. Further investigations could enhance our understanding of cystatin C's role in canine renal health, potentially refining diagnostic and therapeutic approaches in veterinary medicine.

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