www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2018; 7(11): 302-306

www.thepharmajournal.com
Received: 04-09-2018
Accepted: 08-10-2018

Sumit
Department of Veterinary Medicine, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

Parveen Goel
Department of Veterinary Medicine, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

Praveen Kumar
Department of Veterinary Medicine, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

Dinesh Gulia
Department of Veterinary Medicine, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

Ricky Jhambh
Department of Veterinary Medicine, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

Neelesh Sindhu
Veterinary Clinical Complex, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

RN Chaudhary
Department of Veterinary Surgery and Radiology, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

Correspondence
Sumit
Department of Veterinary Medicine, College of Veterinary Sciences, LUVAS, Hisar, Haryana, India

Haematobiochemical and serum electrolytes alteration in dogs with chronic kidney disease

Sumit, Parveen Goel, Praveen Kumar, Dinesh Gulia, Ricky Jhambh, Neelesh Sindhu and RN Chaudhary

Abstract
Dogs with progressive chronic kidney disease (CKD) have haematological alteration of different intensities reflected on the complete blood count parameters. The purpose of this study was to evaluate changes in haemato-biochemical and electrolyte parameters in dogs with CKD. The present study was conducted on 30 dogs suffering from CKD. Major alteration in hematological profile were overall lower levels of hemoglobin (9.15 ± 0.67 g/dl), TEC (4.47 ± 0.30 x 10^6/mm^3), PCV (29.22 ± 2.05 %) values and platelet count (196.23 ± 18.31x 10^3/µL) in all the affected dogs. Affected dogs were showing higher mean TLC count and percentage lymphocytes as compared to reference values. All affected dogs were showing azotemia of various degrees along with mean values of alkaline phosphatase towards higher side (112.65 ± 21.61 U/L), GGT (11.79 ± 1.47 U/L), hyperphosphatemia (11.25 ± 1.17 mg/dl), hyponatremia (140.96 ± 1.69 mmol/L), slight hyperkalemia (5.13 ± 0.22 mmol/L), hypocalcaemia (8.93 ± 0.43 mg/dl). Complete blood count and serum characteristics in CKD provides useful information about the progress of the disease as well as anemia type appreciation offering additional information for therapeutic protocol adjustment for amelioration of induced haemato-biochemical and electrolyte consequences.

Keywords: haematobiochemical, electrolytes alteration, electrolytes alteration

1. Introduction
Chronic kidney disease (CKD) is defined as the presence of structural or functional abnormalities of one or both the kidneys that have been present for an extended period, usually 3 months or longer (Polzin, 2011) [25] or azotemia of renal origin that has been present for more than 2 weeks (Barber, 2003) [1]. CKD is said to be the most common kidney disease in dogs, with prevalence varying from 0.05 to 3.74%. Renal insufficiency induces haematological and serum biochemical alterations in affected dogs. Anemia parallels the degree of renal impairment and its most important cause is failure of renal erythropoietin secretion. Other factors include chronic blood loss, hemolysis and bone marrow suppression by retained uremic factors (Dodds and Nicholls, 1983) [11]. In diagnosis of renal disorders, the determination of non-protein substances especially urea, creatinine and enzymes alkaline phosphatase and gamma-glutamytransferase (Pradhan and Roy, 2012) [27] is very important because significantly increased values are usually the result of accumulation of these substances in blood due to defective kidney elimination (Benjamin, 1985) [26]. Serum creatinine is currently used to stage the severity of CKD in dogs using the IRIS (International Renal Interest Society) staging system with serum creatinine > 1.4 mg/dl being considered azotemic in most dogs. Considering these facts, the present study was planned to investigate haemato-biochemical and electrolyte alterations in dogs suffering from chronic kidney disease.

2. Materials and Methods
The present study was conducted at Veterinary Clinical Complex (VCC), Lala Lajpat Rai University of Veterinary and Animal Sciences (LUVAS), Hisar during period from August (2016) to May (2017). Total 266 cases of dogs suspected for kidney disease were screened based on the patient's history and clinical signs. Furthermore laboratory examination (haemato-biochemical examination, routine urinalysis and urine culture for antimicrobial sensitivity) and imaging techniques (radiology and ultrasonography) were used for confirmatory diagnosis of renal disease. Thirty dogs suffering from chronic kidney disease due to various etiologies were diagnosed on account of clinical signs and elevated serum creatinine (>1.4 mg/dl) and blood urea (>30mg/dl) levels.

For haematobiochemical studies, 6ml of venous blood was collected aseptically from each dog and immediately after collection, 2 ml were transferred in EDTA coated vial and remaining 4 ml blood sample was transferred in clot activator coated plain vials for harvesting serum. The serum was separated by centrifugation at 3000 rpm for 7 min and then stored at -20°C in aliquots for biochemical analysis. Blood samples collected were subjected to haematological examinations comprising of haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), total platelet count (TPC), total leukocyte count (TLC) and differential leukocyte count (DLC) using fully automated haematology cell counter (MS4s, Melet Schloesing Laboratories, France). The serum samples were analyzed for total protein, albumin, globulin, ALT/SGPT, AST/SGOT, total and direct bilirubin, blood urea, serum creatinine, alkaline phosphatase (ALP) and gamma-glutamyltranferase (GGT) by using fully automated random access clinical chemistry analyzer (EM Destiny 180, Erba Diagnostics Mannheim GmbH-Germany). The serum samples were also analyzed for estimation of sodium, potassium and chloride ions using fully automated electrolyte analyzer (Easylyte® expand Na/K/Cl/Ca analyzer). The haemato-biochemical values were compared with standard values available in literature (Kaneko *et al.,* 2008) [16].

3. Results and Discussion

3.1 Haematological profile

The dogs suffering from chronic kidney disease showed lower mean values of haemoglobin, TEC, PCV, MCV, MCH and MCHC than reference values (Table 1). These findings suggest that affected dogs were suffering from microcytic hypochromic anaemia possibly due to various pathogenesis involved such as shortened survival period and haemolysis of red blood cells due to uremia (Ly *et al.,* 2004) [20]; loss of blood in gastrointestinal tract as melena and haematemesis, loss from urinary tract in haematuria due to poor platelet production (Castaldi *et al.,* 1966) [6] and due to deficiency of erythropoietin production by the diseased kidneys (Silverberg *et al.,* 2002) [35]. Similar findings of lower haemoglobin, TEC, PCV were reported by Pradhan and Roy (2012) [27] and Sharma *et al.* (2015) [35]. Results of PCV were in accordance to Couto (2009) [9] and Patil (2011) [24] who demonstrated significantly decreased PCV in CRF dogs ranging from 20 to 30 % and 27.1 to 29.9 %, respectively as compared to the healthy dogs.

Table 1: Haematological parameters (Mean±SE) of dogs affected with chronic kidney disease

Parameter	Mean ± S.E.	Reference value
Hb (g/dl)	9.15 ± 0.67	12-19
TEC (10^6/mm^3)	4.47 ± 0.30	5-7.9
MCV (fl)	65.43 ± 1.04	66-77
PCV (%)	29.22 ± 2.05	35-57
MCH (pg)	20.31 ± 0.49	21-26.2
MCHC (g/dl)	31.22 ± 0.70	32-36.3
Platelets (10^3/µL)	196.23 ± 18.31	211-621
TLC (10^3/mm^3)	16.40 ± 2.73	5-14.1
Lymphocyte (%)	31.03 ± 1.51	8-21
Neutrophils (%)	62.03 ± 2.59	58-85
Monocytes (%)	5.34 ± 1.73	2-10
Eosinophils (%)	1.21 ± 0.21	0-9
Basophils (%)	0.39 ± 0.06	0-1

All the affected dogs revealed lower mean values of platelets count (Table 1) which might be due to insufficient thrombopoietic activity in CKD (Gafter *et al.,*1987) [13] or due to uremic intoxication (Benjamin, 1985) [4]. Similar findings of lower platelets count were recorded by Tilley and Smith (2000) [38], and Sharma *et al.* (2015) [35] in dogs with chronic renal failure. All the affected dogs showed higher mean values of TLC with higher percentage of lymphocytes as compared to reference values. Leukocytosis observed in the affected dogs is in agreement with Robinson *et al*. (1989) [31] who reported higher TLC in dogs with CRF. High TLC has been reported owing to primary inflammatory diseases of urinary system and engrossment of other body system and tissues, similarly reported by Osborne *et al.* (1972) [23].

3.2 Serum biochemical profile

Elevated mean values of urea and creatinine (Table 2) were observed in all the affected dogs as compared to reference value. Reference mean value for urea as per literature is 1.67-3.33 mmol/l (Kaneko *et al.,* 2008) [16] and conversion formula (urea in mg/dl × 0.1665 = urea in mmol/l) was used to convert mmol/l to mg/dl. So, the reference range used for urea was 10-20 mg/dl [Urea (mg/dl) = BUN (mg/dl) ×2.14]. Increased urea and creatinine level in renal failure might be due to marked reduction in glomerular filtration rate (GFR), diminished renal excretion, enhanced tubular absorption of urea and impaired ability of kidneys to excrete proteinaceous catabolites (Osborne *et al*., 1972) [23]. At least 75% loss of functional nephrons occurs before creatinine increases above the reference levels (Watson *et al*., 2002; Lefebvre, 2011) [41, 19]. Similarly findings of increased mean value of BUN and creatinine in dogs with CRF have been recorded by other workers (Kumar, 2013; Pradhan and Roy, 2012; Patil, 2011; Vidyadhar, 2010 and Puri *et al.,* 2015) [18, 27, 24, 40, 19].

Table 2: Serum biochemical parameters (Mean±SE) of dogs with chronic kidney disease.

Parameter	Mean ± S.E.	Reference value
Urea (mg/dl)	320.11 ± 42.23	10-20
Creatinine (mg/dl)	8.61 ± 1.16	0.5-1.5
ALP (µ/L)	112.65 ± 21.61	1-114
GGT (µ /L)	11.79 ± 1.47	1-9.7
SGPT/ALT (µ /L)	56.07 ± 10.12	10-109
SGOT/AST (µ /L)	41.86 ± 9.35	13-15
Total billirubin (mg/dl)	0.28 ± 0.12	0.10-0.50
Direct billirubin (mg/dl)	0.20 ± 0.09	0.06-0.12
Total protein (g/dl)	6.77 ± 0.36	5.4-7.5
Albumin (g/dl)	2.32 ± 0.20	2.3-3.1
Globulin (g/dl)	4.45 ± 0.28	2.4-4.4

Mean values of ALT/SGPT in dogs with chronic kidney disease (Table 2) were within reference range while elevated mean values of AST/SGOT were recorded in affected dogs. ALT is the most liver specific enzyme in the cat and dog while AST is a less specific liver enzyme than ALT, as there are high levels of AST activity in both skeletal muscle and red blood cells (Richter, 2004) [30]. Research advances during the past several decades have contributed much to our understanding of how chronic kidney disease (CKD), its associated comorbidities (*e.g*., diabetes, osteoporosis, cardiovascular disease), its complications (*e.g*., metabolic acidosis, excess glucocorticoid production, inflammation and/or impaired insulin/ insulin-like growth factor-1 signaling) and its therapies (*e.g*., dialysis) all stimulate the loss of skeletal muscle mass (Carrero *et al.,* 2016) [5]. Loss of

the skeletal muscle mass during the CKD might be the reason of increased values of AST observed in the CKD patients.

Mean values of ALP (table 2) were towards the higher side (112.65 ± 21.61 U/L) but within the referenced range (1-114 U/L). Ross *et al*. (2007) [32]; Meyers and Hostetter (2008) [21]; Kumar (2013) [18] and Puri *et al.* (2015) [19] also reported elevated serum ALP in dogs suffering from CKD. Suggestive reason of elevated ALP in CKD might be secondary renal hyperparathyroidism (Center, 1996) [7], which has been reported to be associated with increased mortality in the CRF dogs (Beddhu *et al*., 2009) [3]. Slight elevated mean value of GGT (Table 2) as compared to reference range (1-9.7 U/L) was observed. Finding of elevated serum GGT in present study is in agreement with Heiene *et al*. (1991) [14] and Pradhan and Roy (2012) [27]. Suggestive reason of increased GGT value in CKD might be its more release from the damaged renal tubular cells (Pradhan and Roy, 2012) [27]. Targhera *et al.* (2010) [37] reported a strong independent relationship of increased serum GGT concentrations with CKD. Therefore, serum GGT may be considered as an early predictor for the development of CKD (Ryu *et al*., 2007) [33].

Overall mean values of total bilirubin (Table 2) were within the reference range while higher value of direct bilirubin was observed. Elevated mean values of total bilirubin were also observed by Beckel *et al.* (2005) [2] in dogs suffering from renal failure due to leptospirosis. Mild to moderate bilirubin in urine of dogs with CRF has been observed (Srivastava *et al.,* 2012; Kumar, 2013) [36, 18], which may be due to low threshold for bilirubin (Duncan *et al.,* 1994) [12] or due to concurrent polysystemic etiology of renal dysfunction including liver and bile duct (Osborne *et al.*,1972) [23]. Mean values of total protein (Table 2) was within reference range while mean values of albumin was towards the lower side in all affected dogs as compared to reference range. Hypoalbuminemia might be observed due to gastrointestinal or renal protein loss of albumin. Similar findings were also observed by Pradhan and Roy (2012) [27] whereas Kandula and Karlapudi (2014) [15] reported hypoproteinemia (3.26 ±1.84 g/dl) and hypoalbuminemia (1.38 ±1.28 g/dl) in dogs with chronic kidney disease. Mean values of globulin (Table 2) in were towards the higher side of reference range and that might be the suggestive reason for normal level observation of total protein. The progress of an infection is usually associated with marked changes in the serum proteins, production of acute phase proteins (APP's) by liver and most of the APP's are globulins (Kaneko *et al.,* 2008) [16]. Thereby, the concurrent infection might be the reason of increased globulin and total protein level.

Overall mean value of serum potassium levels was towards the higher side of reference range in affected dogs as shown in table 3, which is in consistent with findings of Patil (2011) [24] and Puri *et al*. (2015) [19] who observed high serum potassium level in dogs affected with CRF. Overall slight hyponatraemia (Table 3) was observed in affected dogs. Non-significant changes has been reported in the mean value of sodium in cases suffering from CRF (Meyers and Hostetter, 2008; Vidyadhar, 2010; Patil, 2011; Kumar, 2013) [21, 40, 24, 18]. Suggestive reasons of hyponatremia include hypotension, pain, and renal injury which activate the sympathetic nervous system, renin angiotensin-aldosterone system and antidiuretic hormone release (Prowle *et al*., 2010) [28], which results in decreased renal perfusion, decreased GFR and increased proximal tubular reabsorption of sodium and water in advanced renal failure (DiBartola, 2006) [10].

Table 3: Serum electrolyte parameters (Mean±SE) of dogs affected with chronic kidney disease

Parameter	Mean ± S.E.	Reference value
Na^+ (mmol/L)	140.96 ± 1.69	142-152
K^+ (mmol/L)	5.13 ± 0.22	3.9-5.1
Cl^- (mmol/L)	117.39 ± 1.47	110-124
Total Calcium (mg/dl)	8.93 ± 0.43	9.1-11.7
Phosphorus (mg/dl)	11.25 ± 1.17	2.9-5.3

Results of the present study revealed slight hypocalcaemia (Table 3) in affected dogs. Pradhan and Roy (2012) [27] and Kumar (2013) [18] also reported highly significant decrease in the mean value of calcium in cases suffering from CRF. Similar findings were also observed by Kumar (2013) [18] and Ross *et al.* (2007) [32] in stage II, III and IV of CRF. Suggestive reason of hypocalcaemia may be the less absorption of calcium in the intestine due to less production of calcitriol from the damaged kidney (Nagode *et al*., 1996) [22]. Elevated mean value of Phosphorus (Table 3) was observed in all affected dogs as compared to reference value. Similar findings were also reported by Kandula and Karalpudi (2015) and Tivanana (2015) [39]. Further mean values observed were in the agreement with the findings of Chew and Gieg (2006) [8]; Vidyadhar (2010) [40]; Patil (2011) [24]; Kumar (2013) [18] and Puri *et al.* (2015) [19]. Suggestive reason for hyperphosphatemia is declining kidney function because the kidneys are the primary route of phosphorus excretion and its consequences results in phosphorus retention. In chronic kidney disease, serum phosphorus concentrations typically parallel to the serum urea nitrogen concentrations and it correlated significantly with the severity of disease. Thus, hyperphosphatemia is common in azotaemia, but not in non-azotemic renal disease (Polzin, 2010) [26]. Hyperphosphatemia promotes progressive renal lesions and was found to be associated with increased morbidity and mortality in CRF dogs (Kestenbaum *et al*., 2005) [17]. Dogs with serum phosphorous range 6.6 to 7.8 mg/dL have been reported to have 13% higher mortality than dogs with phosphorous levels within the reference range (Polzin, 2010) [26].

4. Conclusions

Dogs with chronic renal failure showed abnormal haematological and biochemical parameters. In chronic renal failure, impaired production of erythropoietin due to loss of renal parenchyma, increase haemolysis, suppression of bone marrow erythropoiesis, hematuria and gastrointestinal blood loss were associated with anemia. Rise in biochemical and electrolyte parameters such as BUN, serum creatinine and phosphorus was directly proportional to the severity of disease and loss of the renal function, while inversely proportional to the prognosis of the disease. Complete blood count and serum characteristics provides useful information about the progress of the disease as well as anemia type appreciation offering additional information for therapeutic protocol adjustment for amelioration of induced haemato-biochemical and electrolyte consequences.

5. References

1. Barber P. Diagnosis and management of chronic renal failure in the cat. In Practice. 2003; 25:306-313.
2. Beckel NF, O'Toole TE, Rozanski EA, Labato MA. Peritoneal dialysis in the management of acute renal failure in 5 dogs with leptospirosis. Journal of Veterinary Emergency and Critical Care. 2005; 15(3):201-205.

3. Beddhu S, Ma X, Baird B, Cheung AK, Greene T. Serum alkaline phosphatase and mortality in African Americans with chronic kidney disease. Clinical Journal of the American Society of Nephrology. 2009; 4(11):1805-1810.
4. Benjamin MM. Outline of Veterinary Clinical Pathology. 3rd edn. The IOWA State University Press. Ames. IOWA. USA. 1985; 5-162:175-228.
5. Carrero JJ, Johansen KL, Lindholm B, Stenvinkel P, Cuppari L, Avesani CM. Screening for muscle wasting and dysfunction in patients with chronic kidney disease. Kidney International. 2016; 90(1):53-66.
6. Castaldi PA, Rosenberg MC, Stewart JH. The bleeding disorder of uremia: A qualitative platelet defect. The Lancet. 1966; 288(7454):66-69.
7. Center S. Diagnostic procedures for evaluation of hepatic disease. In: Grant Guilford W, Center SA, Strombeck DR, *et al*, eds. Strombeck's small animal gastroenterology. 3rd ed. Philadelphia, Pa: WB Saunders Co. 1996, 136-143.
8. Chew DJ, Gieg JA. Fluid therapy during intrinsic renal failure. In: DiBartola S. P. (eds). Fluid, electrolyte and acid- base disorders in small dog practice. Saunders, St Louis, 2006, 518-540.
9. Couto CG. Anemia of renal disease. In: Nelson, R. W. and C. G. Couto, Ed: Small Dog Internal medicine, 4th Ed. Elsevier, 2009, 1220.
10. DiBartola SP. Disorders of sodium and water: Hypernatremia and hyponatremia. In: DiBartola, S. P. Ed: Fluid, Electrolyte and Acid-Base Disorders in small animal Practice, 3rd ed. Elsevier Saunders, Philadelphia, 2006, 47-79.
11. Dodds A, Nicholls M. Haematological aspects of renal disease. Pub Med – index for medline. 1983; 11(4):361-368.
12. Duncan JR, Prasse KW, Mahaffey EA. Veterinary Laboratory Medicine: Clinical Pathology. 3rd ed. Iowa State University Press, Ames, 1994, 162-183.
13. Gafter U, Bessler H, Malachi T, Zevin D, Djaldetti M, Levi J. Platelet count and thrombopoietic activity in patients with chronic renal failure. Nephron. 1987; 45(3):207-210.
14. Heiene R, Biewenga WJ, Koeman JP. Urinary alkaline phosphatase and gamma glutamyl transferase as indicators of acute renal damage in dogs. Journal of Small Animal Practice. 1991; 32:521-524.
15. Kandula S, Karlapudi SK. Prevalence of renal disorders in dogs-a clinical study. International Journal of Agricultural Sciences and Veterinary Medicine. 2014; 2(3):146-148.
16. Kaneko JJ, Harvey J, Bruss ML. Serum proteins and dysproteinemias. In: Clinical biochemistry of domestic dogs. Academis press, New York, 2008.
17. Kestenbaum B, Sampson JN, Rudser KD, Patterson DJ, Seliger SL, Young B *et al*. Serum phosphate levels and mortality risk among people with chronic kidney disease. Journal of American Society of Nephrology. 2005; 16(2):520-528.
18. Kumar M. Studies on urinary tract disorders in dogs in Jammu. A thesis submitted to Division of Veterinary Medicine Sher-E-Kashmir University of Agricultural Sciences and Technology af Jammu, main campus. Chatha, Jammu 180009, 2013.
19. Lefebvre H. Renal function testing. In: Nephrology and Urology of Small Dogs. Eds J. Bartges and D. Polzin. Wiley-Blackwell, Ames, IA, USA, 2011, 91-96.
20. Ly J, Marticorena R, Donnelly S. Red blood cell survival in chronic renal failure. American Journal of Kidney Diseases. 2004; 44(4):715-719.
21. Meyers T, Hostetter T. Pathophysiology of uremia. Brenner BM The kidney. Saunders Philadelphia, 2008, 1681-1696.
22. Nagode LA, Chew DJ, Podell M. Benefits of calcitriol therapy and serum phosphorous control in dogs and cats with chronic renal failure: both are essential to prevent or suppress toxic hyperparathyroidism. Veterinary Clinics of North America: Small Animal Practice. 1996; 26(6):1293-1330.
23. Osborne CA, Low DG, Finco DR. Canine and Feline Urology. W.B. Saunders company. Philadelphia, 1972, 3-10, 39-84.
24. Patil SB. Therapeutic management of canine azotemia with Hemodialysis and evaluation of hemodialyzer clearance. Thesis submitted to Bombay Veterinary College, Mumbai, Maharashtra Dog and Fishery Sciences University, Nagpur (India), 2011.
25. Polzin DJ. Chronic kidney disease in small dogs. Veterinary Clinics of North America: Small Dog Practice. 2011; 41(1):15-30.
26. Polzin DJ. Chronic kidney disease. In: Ettinger SJ, Feldman EC, editors, Textbook of veterinary internal medicine, St Louis (MO): Saunders Elsevier. 2010; 2:1990-2021.
27. Pradhan NR, Roy S. Chronic renal failure in dogs and its management. Indian Journal of Canine Practice. 2012; 4(2):88-92.
28. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nature Reviews Nephrology. 2010; 6(2):107-115.
29. Puri D, Dua K, Sood NK, Randhawa S, Dhaliwal PS. Study of renal dysfunctions in geriatric dogs. Veterinary Practitioner. 2015; 16(1):44-46.
30. Richter K. Current evaluation of liver disease (VET – 194). In Western Veterinary Conference, 2004.
31. Robinson WF, Shaw SE, Stanley B, Huxtable CR, Watson ADJ, Friend SE, Mitten R. Chronic renal disease in Bull terriers. Australian Veterinary Journal. 1989; 66(7):193-195.
32. Ross SJ, Osborne CA, Lekcharoensuk C. A case-control study of the effects of nephrolithiasis in cats with chronic kidney disease. Journal of American Veterinary Medical Association. 2007; 230:1854-1859.
33. Ryu S, Chang Y, Kim DI, Kim WS, Suh BS. γ-Glutamyltransferase as a predictor of chronic kidney disease in nonhypertensive and nondiabetic Korean men. Clinical chemistry. 2007; 53(1):71-77.
34. Sharma A, Ahuja A, Srivastava M, Kachhawa JP. Haemato-biochemical changes in Dogs suffering from chronic renal failure. Indian Journal of Canine Practice. 2015; 7(2):102-107.
35. Silverberg DS, Wexler D, Blum M. The correction of anemia in severe resistant heart failure with erythropoietin and intravenous iron prevents the progression of both the heart and the renal failure and markedly reduces hospitalization. Clinical Nephrology. 2002; 58(1):37-45.
36. Srivastava MK, Gaikwad RV, Kachhawaha S, Srivastava A, Purohit S. Comparative study of urinalysis in healthy and renal failure dogs. Veterinary Practitioner. 2012;

13(2):245-247.
37. Targhera G, Kendrick J, Smits G, Chonchol M. Relationship between serum gamma-glutamyltransferase and chronic kidney disease in the United States adult population. Findings from the National Health and Nutrition Examination Survey 2001–2006. Nutrition, Metabolism and Cardiovascular Diseases. 2010; 20(8):583-590.
38. Tilley LP, Smith FWK. 5-Minute Veterinary Consult, Lippincott Williams & Wilkins, 2000.
39. Tivanana MR. Clinico-diagnostic and therapeutic studies on chronic kidney disease in dogs, Doctoral thesis submitted to Gannavaram Shri Venkateshwara veterinary university, Tirupati, 2015.
40. Vidyadhar GK. Management of canine azotemia by employing haemodialysis and conventional therapeutic methods. Thesis submitted to Bombay Veterinary College, Mumbai, Maharashtra Dog and Fishery Sciences University, Nagpur (India), 2010.
41. Watson ADJ, Lefebvre HP, Concordat D, Laroute V, Ferre JP, Braun JP *et al.* Plasma exogenous creatinine clearance test in dogs: Comparision of other methods and proposed limited sampling strategy. Journal of Veterinary Internal Medicine. 2002; 16:22-33.