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Assessment of serum prooxidant and antioxidant minerals and electrolytes in stage 3 and stage 4 of chronic kidney disease in dogs#

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Abstract

Chronic kidney disease (CKD) is the most commonly recognised form of kidney disease in dogs and cats. Dogs with the clinical signs suggestive of renal failure were screened and eight dogs each with stage 3 and stage 4 of CKD as per International Renal Interest Society were selected based on serum creatinine level. All the animals were subjected to detailed clinical examination and assessment of sodium, potassium, bicarbonate and serum minerals viz. copper, iron, zinc and selenium. Major clinical signs recorded were anorexia/hyporexia and dehydration in stage 3 and vomiting, anorexia/hyporexia, pale mucous membrane and cachexia in stage 4 animals. Stage 3 animals showed reduction in bicarbonate levels and hypokalemia and stage 4 animals showed metabolic acidosis with hyperkalemia. Estimation of serum mineral levels showed a significant decrease in zinc levels in stage 4 and an increase in copper levels in stage 3 and stage 4 animals.

Keywords: C*hronic kidney disease, minerals, electrolytes*

Renal failure is one of the most leading causes of death in dogs. Chronic kidney disease affects dogs of all ages, but more commonly older dogs. It is a progressive disease in dogs. The major complications of CKD are proteinuria, hypertension and electrolyte imbalances. Oxidative stress plays an important role in progression of kidney disease and many of the trace elements are involved in the oxidant-antioxidant balance. Iron and copper are prooxidant minerals while zinc and selenium are considered to be antioxidant in its effect. Selenium is a cofactor in maintaining the activity of glutathione peroxidase and zinc is considered as a cellular antioxidant as it is a component of superoxide dismutase whereas copper and iron catalyze the generation of reactive oxygen species (Shih et al*.,* 2012). The present study aims to evaluate these mineral levels in stage 3 and stage 4 of CKD in dogs.

Material and methods

The dogs that were presented to University Veterinary Hospital, Mannuthy and Kokkalai, irrespective of breed and gender and above one-year age with the clinical signs suggestive of renal failure were screened for the study. Sixteen

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animals were selected and grouped into two: group I included animals with stage 3 CKD and group II included animals with stage 4 CKD based on serum creatinine levels as per International Renal Interest Society guidelines, 2023. Six apparently healthy animals served the control.

Blood gas analysis was performed with the blood collected in heparin vial using the EPOC blood gas analyzer. Serum biochemical parameters *viz* creatinine, total protein and albumin were estimated using Hospitex-Screen Master T semi-automatic biochemical analyzer. For the estimation of serum minerals, copper, iron, zinc and selenium, the serum sample was prepared by diluting 1ml serum in 9ml 1% nitric acid solution and read by flame atomic absorption spectrometry in PerkinElmer Atomic Absorption Spectrometer PinAAcle 900H (Shih *et al.,* 2012). Statistical analysis of the various parameters was done using SPSS 24.0 software.

Results and discussion

In the studied population, mature adult dogs with age ranging two to six years represented four animals out of eight in stage 3 and five out of eight in stage 4 CKD cases. Age group classification was done according to Harvey (2021). Major clinical signs recorded in group I animals include anorexia/hyporexia and dehydration followed by pale mucous membrane, vomiting, cachexia, dullness, poor hair coat, reduction in water intake, polyuria, pasty faeces and halitosis. Those in group II animals were vomiting, followed by anorexia/hyporexia, pale mucous membrane, cachexia, dullness, dehydration, pasty faeces, halitosis, oral ulcers, polyuria and polydipsia. This is consistent with the findings reported by Polzin (2011), O'Neill et al. (2013), and Geetika et al. (2024). Jayananthan et al. (2021) attributed the presence of oral ulcers and uraemic breath in stage 4 renal disease to ammonia, a byproduct of bacterial urea degradation. According to Lippi et al. (2022), cachexia associated with renal failure results from inadequate energy intake combined with enhanced protein catabolism. In dogs with CKD, polyuria may result from impaired renal concentrating ability, leading to increased urine output; the consequent dehydration stimulates compensatory polydipsia (Geetika et al., 2024). Westropp and Lulich (2007) reported that lethargy observed in CKD patients is associated with dehydration, disturbances in electrolyte balance, anaemia and the accumulation of uraemic toxins.

Comparison of blood gas and electrolyte analysis depicted in table 1 revealed a significant ($p<0.05$) reduction in blood pH in group II animals and bicarbonate levels showed a significant($p<0.05$) reduction in both the groups when compared to control animals. This was in accordance with the findings of Benedito et al. (2025). Neethu (2022) and Lippi et al. (2023) also recorded a

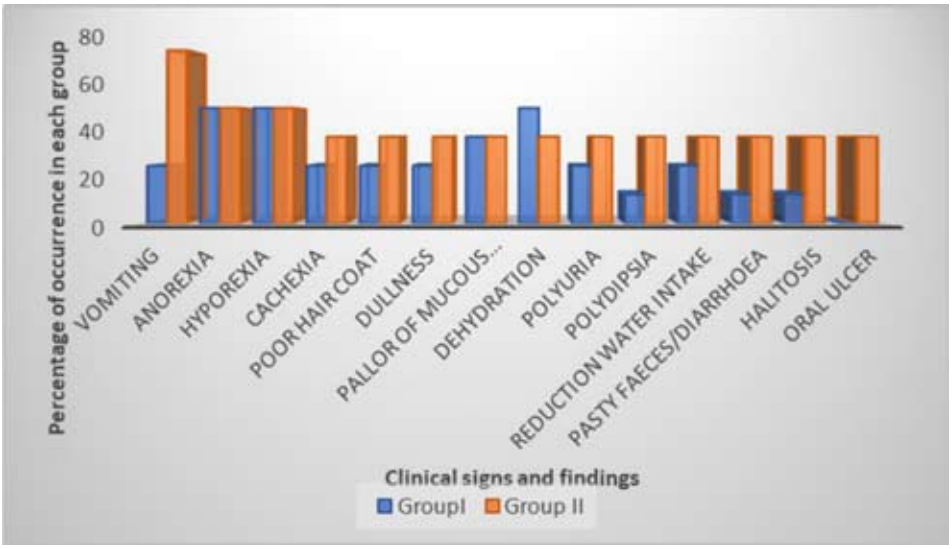

Fig. 1 Clinical signs and findings in group I and group II animals

Table 1. Comparison of parameters of blood gas analysis in group I, II and healthy animals

Variable	Healthy control (n=6) Mean ± SE	Group I (n=8) Mean ± SE	Group II (n=8) Mean ± SE	F value	p value
pH	7.46 ± 0.02[a]	7.36 ± 0.05[a, b]	7.28 ± 0.05[b]	3.573*	0.048
Bicarbonate (mmol/L)	20.38 ± 0.72[a]	16.61 ± 2.39[b]	11.78 ± 1.76[b]	4.858*	0.020
Na^+ (mmol/L)	150 ± 1.69	146.13 ± 3.31	139.75 ± 2.64	3.307	0.059
K^+ (mmol/L)	3.72 ± 0.07[a]	3.54 ± 0.34[b]	4.71 ± 0.33[c]	4.562*	0.024

*Significant $p<0.05$

Table 2. Comparison of serum minerals in group I, II and healthy animals

Variable	Healthy control(n=6) Mean ± SE	Group I (n=8) Mean ± SE	Group II (n=8) Mean ± SE	F value	p value
Iron (µg/dL)	132.33 ± 22.44	156.34 ± 26.07	85.52 ± 20.495	2.555	0.104
Copper (µg/dL)	60.5 ± 3.905[a]	207.25 ± 40.89[b]	146.44 ± 23.20[b]	5.647*	0.012
Zinc (µg/dL)	105.5 ± 17.21[a]	105.125 ± 83.32[a]	56.3 ± 11.53[b]	5.504*	0.013
Selenium (mg/L)	0.715 ± 0.32	1.36 ± 0.36	1.39 ± 0.36	0.936	0.410

*Significant p<0.05

reduced bicarbonate levels in CKD dogs. Lippi et al. (2023) observed a higher frequency of decreased bicarbonate levels as the disease advanced. This is attributed to the reduced net renal acid excretion and reduced ammonia genesis due to the inability to uptake glutamine at the level of proximal tubules. No significant difference could be noticed in sodium concentration which was in accordance with the findings of Ribeiro et al. (2020) and contrary to Oburai et al. (2015). Serum sodium concentration can be variable in kidney diseases as hypernatremia occurred before fluid administration, which suggest excessive free water loss and hyponatremia can occur due to vomiting and pancreatitis (Langston, 2017). There was a significant decrease in the potassium levels in group I animals and group II animals showed a significant increase when compared to the control animals. Langston (2017) noted that hypokalemia is often associated with polyuric CKD and may be aggravated by vomiting, prolonged anorexia, or loop diuretic use. In contrast, hyperkalemia may develop in renal failure with severe metabolic acidosis due to extracellular potassium shift.

Serum concentrations of iron, copper, zinc, and selenium were compared (Table 2). Serum iron levels in group I and group II animals did not differ significantly from those of healthy animals. This aligns with the findings

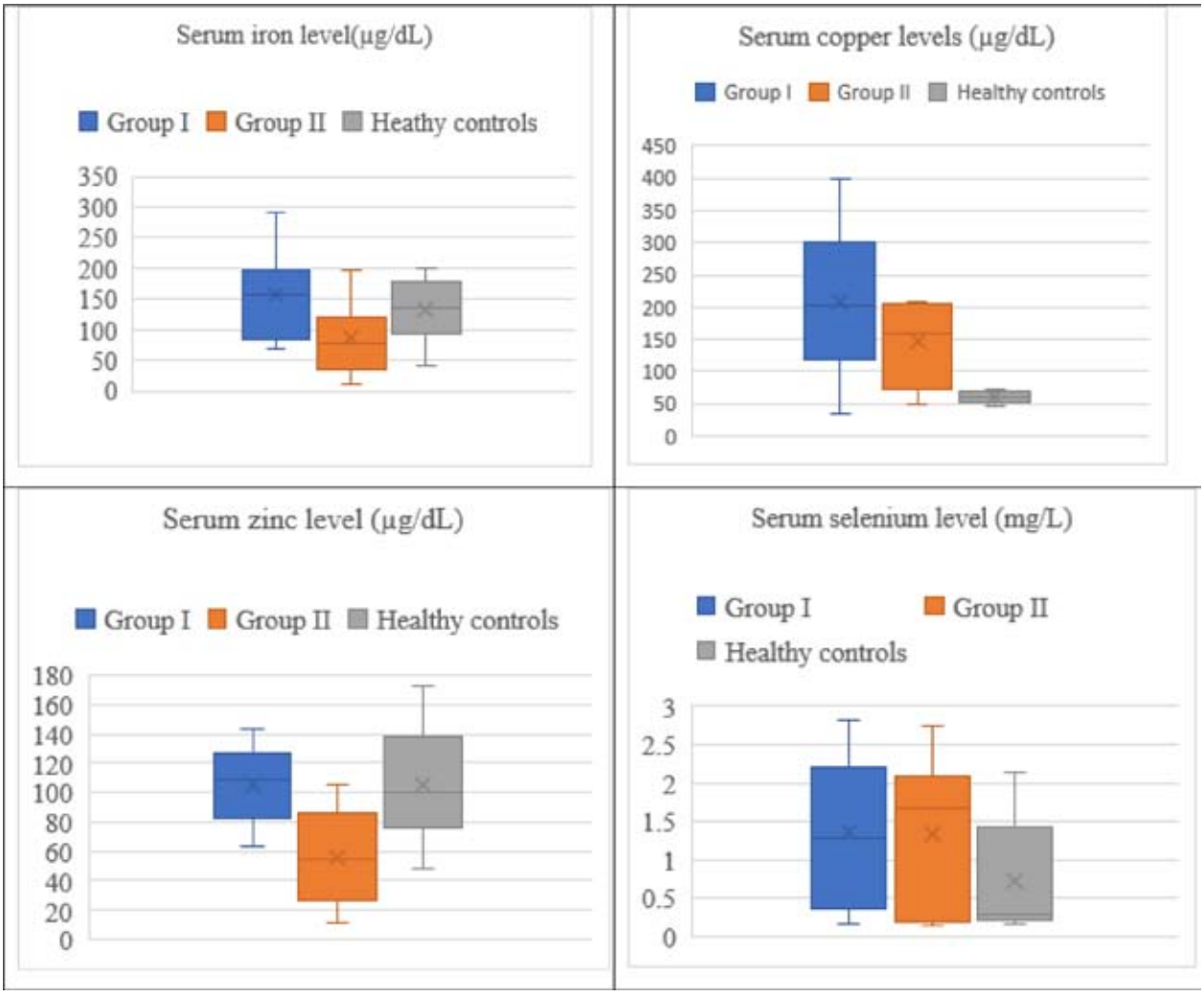

FIG 1 Box and whisker representation of serum mineral levels in group I, group II and healthy animals

Table 3. Comparison of serum biochemical parameters in group I, II and healthy animals

Variable	Healthy control (n=6) Mean ± SE	Group I (n=8) Mean ± SE	Group II (n=8) Mean ± SE	F value	p value
Creatinine (mg/dL)	1.132 ± 0.063[a]	3.91 ± 0.26[b]	15.07 ± 2.17[c]	28.55**	0.00
Total protein (g/dL)	6.23 ± 0.41	6.3 ± 0.36	6.25 ± 0.37	0.01	0.99
Albumin (g/dL)	3.12 ± 0.22[a]	2.84 ± 0.235[a, b]	2.296 ± 0.12[b]	4.53*	0.02

**Significant p<0.01, *Significant p<0.05

of Bhamarasuta et al. (2021), who explained that iron is predominantly bound to transport proteins, with serum iron accounting for less than 0.1% of total body iron. In contrary to this, Jithin et al. (2022) noticed a significant decrease in iron levels in dogs with CKD and associated anaemia. Two animals in group II were found to be deficient in serum iron level, which could be due to reduced intestinal absorption or functional iron deficiency. While, three animals in group I and one animal in group II showed an increase in serum iron. According to Xie et al. (2022), iron overload in CKD might lead to ferroptosis that mediate renal cell death, contributing to renal fibrosis. There was a significant increase in the copper levels in group I and group II animals. According to Gembillo et al. (2022), an elevation in copper concentration in blood causes renal deposition that results in interstitial damage and excretion of excess copper through the damaged renal tubules, together contributed to the progression of renal dysfunction in human patients with advanced CKD. The present study showed a significant decrease in the serum zinc levels in group II animals which could be attributed to enhanced urinary excretion as explained by Pereira et al. (2020). Cedeno et al. (2020) proposed that albumin is the primary plasma protein responsible for zinc transport, and that zinc concentrations decline during acute phase responses due to hypoalbuminemia. As depicted in table 3, serum albumin values in group II differed significantly from that of group II and healthy animals. Mortality was recorded in the animals with reduced serum zinc levels. There was no significant difference in the selenium levels in both the groups when compared to healthy animals. A similar finding was reported by Krofic Zel et al. (2014) in cats with CKD. However, Zachara et al. (2016) reported a reduction in serum selenium concentration in humans

loss in CKD patients. The increased level of prooxidant mineral, copper and the decrease antioxidant mineral, zinc, might have contributed to the disease progression by adding to oxidative damage to renal tissue with end stage renal disease and related it to lower protein intake and increased urinary protein

Conclusion

The major metabolic derangement noticed in CKD dogs were metabolic acidosis and potassium imbalance. The present study revealed an increase in copper levels and a decrease in zinc levels in chronic kidney disease in dogs which might have contributed to oxidative damage of renal tissues and further disease progression. Assessing mineral concentrations in CKD is clinically significant, as it helps to guide appropriate therapeutic strategies that may slow disease progression.

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Conflict of interest

The authors declare no conflicts of interest.

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