



Evaluation of electrocardiographic and serum biochemical changes in arrhythmias associated with renal diseases of dogs[#]

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Abstract

The present study was conducted to investigate electrocardiographical (ECG) and haemato-biochemical changes in arrhythmia associated with renal diseases in dogs. The dogs with renal affections confirmed through appropriate diagnostic methods were selected and screened for arrhythmia. The ECG and haemato-biochemical parameters of twenty dogs with arrhythmia were compared with that of the control group and ECG parameters were statistically correlated with the haemato-biochemical parameters for correlation studies. It was found that the occurrence of arrhythmia was 51.2 per cent in renal diseases. Arrhythmia was more predominant in dogs with chronic kidney disease (CKD) followed by acute kidney injury (AKI). Sinus arrhythmia followed by first-degree AV block and wandering pacemaker were the common types of arrhythmias observed. A significant increase in R-R interval and a decrease in heart rate was noticed in comparison. The haemato-biochemical analysis revealed anaemia, leukocytosis with neutrophilia, elevated blood urea nitrogen (BUN), creatinine and magnesium level. A significant positive correlation was noticed between haemoglobin, volume of packed red cells (VPRC) and red blood cell count (RBC) with T amplitude and, creatinine and BUN levels with corrected Q-T interval. A significant negative correlation was noticed between VPRC, RBC and haemoglobin with the corrected QT interval. The present study revealed ECG and haemato-biochemical parameters had a significant role in renal diseases in dogs which might help in the early diagnosis and proper management of arrhythmia associated with renal diseases.

Keywords: Renal disease, Arrhythmia, electrocardiography, correlation studies

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The term arrhythmia is used to describe the variation in the normal rate, rhythm, and electrical conductivity in the heart. Most kidney diseases have direct or indirect cardiovascular effects, which include systemic hypertension, left ventricular hypertrophy, fluid volume dysregulation and electrolyte imbalances. In many cases, there is a causal relationship, with renal dysfunction promoting arrhythmias and arrhythmias exacerbating renal dysfunction (Keller *et al.*, 2016). Bagshaw *et al.* (2013), observed that canine acute kidney injury (AKI) usually resulted in arrhythmias and cardiac damage due to the production of pro- and anti-inflammatory cytokines, as well as the activation of the sympathetic and renin-angiotensin-aldosterone systems. The metabolic abnormalities linked with renal diseases, such as acidaemia, hyperkalemia, hypocalcaemia, hyperphosphataemia, azotaemia, and anaemia, could have a significant impact on the electrical activity and functioning of the myocardium. In the case of chronic kidney disease (CKD), left ventricular hypertrophy and persistent systemic hypertension results in arrhythmia. Electrolyte imbalance and dehydration associated with kidney diseases can be easily and quickly identified using ECG which will enable early treatment. Minor reductions in kidney function could cause electrophysiological changes, properties of the myocardium, as well as an increased risk of ventricular arrhythmias and sudden cardiac death (Mozos, 2014). In the context of renal dysfunction, electrophysiological monitoring proved crucial, especially during treatment, to identify cardiovascular effects early and give the patient a better prognosis. As of now, only a few studies report the correlation between cardiac affection and canine kidney disease. Hence this study was carried out to identify the ECG pattern and haemato-biochemical alterations linked with arrhythmia in canine renal disorders and to find out the existence of a correlation between arrhythmia and renal diseases in dogs.

Materials and methods

Selection of animals

The present study was carried out

using the facilities available at the Department of Veterinary Clinical Medicine, Ethics and Jurisprudence, College of Veterinary and Animal Sciences, Mannuthy, Kerala, India. Dogs presented to the University Veterinary Hospitals at Kokkalai and Mannuthy irrespective of their age, breed and sex with signs of renal affections including polyuria, anuria, dysuria, halitosis, and elevated BUN and creatinine levels exceeding 25 mg/dL and 1.5 mg/dL, respectively were selected for the study. The selected animals were screened for the presence of arrhythmia and a minimum of twenty such animals with arrhythmia were selected for the present study. Ten apparently healthy dogs with normal clinico-physiological parameters were chosen for the study as control animals for comparison.

Electrocardiography

A 12-lead standard ECG recorder, BPL CARDIART-6108[®] machine under all standard prescribed conditions was used for the present study. Animals were subjected to three-minute electrocardiography using standard bipolar limb leads and augmented unipolar limb leads. The electrocardiograph had been standardized 1 cm = 1 mV so that each small box on the vertical axis equals 0.1 mV. The tracings were recorded at a paper speed of 25mm/sec so each small box on the horizontal axis equals 0.04 seconds. The measurements of waveforms in lead-II were included in this study. Electrocardiograms thus obtained were observed for the presence of ECG abnormalities conforming to arrhythmia.

Haemato-biochemical parameters

Haematological parameters namely haemoglobin, volume of packed red cells (VPRC), red blood cell count (RBC), white blood cell count (WBC), neutrophil, lymphocyte, monocyte and platelet count using Mythic 5 Vet Prohaematology analyser (Cormay Diagnostics, Poland). Serum creatinine, blood urea nitrogen (BUN), alanine phosphatase (ALP) and alanine aminotransferase (ALT) were estimated using the specific standard assay kits provided by Spinreact S. A. U. in Master T – Semi-automatic Analyser (Hospitex International, Italy). Serum potassium, calcium, magnesium, and CK-MB were estimated based on colorimetric method using standard kits Elyte 2 kit (Crest

Biosystems), Labkit Calcium – Arsenazo III (Chemelex, S. A.), Labkit Magnesium Calmite – EGTA (Chemelex, S. A.) and CK MB (NAC activated) (Coral Clinical Systems) respectively in fully automated biochemical analyser (M/s Selectra Pro S Lite, Netherlands) as per manufacturer's instructions.

Statistical analysis

Statistical analysis of data generated in the study was analysed using GraphPad Prism Version 5.01. Haemato-biochemical and ECG parameters were compared with the control group using independent t-test. Haemato-biochemical values and ECG parameters were correlated using Pearson's correlation method.

Results and discussion

Occurrence

Out of 35 animals screened for the presence of arrhythmia, 20 were selected. The per cent of occurrence of arrhythmia was 51.2 per cent in dogs with renal disorders. The common clinical conditions with arrhythmia were chronic kidney disease (CKD) (60%) followed by acute kidney injury (AKI) (35%) per cent and urinary tract infections (5%). Manev (2021) documented arrhythmia in 25 per cent of dogs with CKD. Perini-Perera *et al.* (2021) and Keller *et al.* (2016) observed more arrhythmias in dogs with AKI due to infectious diseases.

Electrocardiographic studies

Sinus arrhythmia was observed more frequently in 17.91 per cent (Fig. 1), followed by first-degree atrioventricular block (13.43%), prolonged QT interval in 8.96 per cent (Fig. 5), 7.46 per cent each of P mitrale (Fig. 4), increased QRS duration and wandering pacemaker (WPM), elevated T wave in 5.97 percent (Fig. 3), 4.48 percent each of low R amplitude (Fig. 5) and sinus block (Fig. 2), unifocal VPC in 2.99 (Fig. 6), 1.49 percent each of P pulmonale, atrial ectopic beat, ventricular ectopic beat, ventricular bigeminy, multifocal VPC, notched QRS, ventricular escape rhythm, atrial fibrillation (Fig. 7), notched P wave, ST coving (Fig. 4), second-degree sinoatrial block – type I and II and electrical alternans. Uremic

neuropathy and sympathetic overactivity associated with CKD would result in arrhythmia (Aktar *et al.*, 2022). Conduction abnormalities like first-degree AV block, sinus block and increased QRS duration which were presented in both CKD and AKI might be due to elevated hyper-adrenergic stage and vagal response which would lead to conduction delay (Elias *et al.*, 2004).

Elevated potassium was found in five cases which were associated with elevated T wave, first-degree AV block, prolonged QRS duration, junctional rhythm, and ST segment changes. Elevated potassium was noticed in those dogs presented with decreased renal elimination associated with anuria or oliguria in the present study. Elevated potassium concentration might potentiate vagal action and reduce the resting potential to inhibit the propagation of impulses which resulted in bradycardia and cardiac arrest (Varshney, 2020). In the present study, hypokalemia resulted in prolonged P duration in three dogs, similar to the findings of Korzets *et al.* (2001). Six dogs with CKD had hypokalemia associated with prolonged Q-T interval. Hypokalaemia caused hyperpolarization of nerve and muscle fibre membranes and manifested as delayed or abnormal repolarization, increased automaticity, and increased duration of action potential (Tilley and Smith, 2007).

Ventricular arrhythmias such as ventricular ectopic beat, VPC and atrial arrhythmias like atrial fibrillation, and atrial ectopic beat were observed. This was in accordance with Manev (2021). In this study, four dogs with the presence of VPC and one with atrial fibrillation had sudden cardiac death. The two life-threatening arrhythmias reported in canines were VPC and atrial fibrillation (Vishnurahav *et al.*, 2018). Dogs with end-stage renal failure might have endothelial dysfunction and inflammation which resulted in perfusion defect and fibrosis of atrial and ventricular tissue that have contributed to arrhythmia and sudden cardiac death in the present case (Ferreira *et al.*, 2015, Akoum *et al.*, 2019). Low amplitude R wave was noticed in three dogs who died during the treatment. Metabolic derangements associated with uraemia in end-stage CKD

such as hypocalcaemia, hypoproteinaemia and hyperkalaemia were the precipitating factor for pericardial effusion and associated low R amplitude in ECG (Alpert *et al.*, 2003; Ravi *et al.*, 2018).

The mean values of ECG parameters are depicted in Table 1. Statistically, a significant increase in RR interval and a decrease in heart rate were noticed when compared to the control group. In the case of uremic patients,

Table 1. Mean values of ECG parameters of dogs with renal diseases

Sl. No	Parameters	Control (n=10)	Diseased group (n=20)	t-value	p-value
1	Rate (bpm)	112.5 ± 3.43	91.38 ± 6.75	2.12*	0.04
2	P amplitude (mV)	0.20 ± 0.02	0.19 ± 0.03	0.22	0.82
3	P duration (sec)	0.04 ± 0.001	0.04 ± 0.003	1.01	0.32
4	R amplitude (mV)	1.09 ± 0.10	1.08 ± 0.14	0.04	0.96
5	QRS duration (sec)	0.04 ± 0.002	0.05 ± 0.003	1.37	0.18
6	T amplitude (mV)	0.18 ± 0.02	0.30 ± 0.05	1.71	0.09
7	T duration (sec)	0.05 ± 0.005	0.06 ± 0.004	0.95	0.35
8	PR interval (sec)	0.09 ± 0.005	0.12 ± 0.01	1.35	0.18
9	Corrected QT interval (sec)	0.24 ± 0.007	0.26 ± 0.01	1.19	0.24
10	RR interval (sec)	0.54 ± 0.02	0.81 ± 0.06	3.02**	<0.001

*Significant at 0.05 level and ** Significant at 0.01 level



Fig. 1. Lead II, sensitivity 10mm/mv, speed 25mm/s, Sinus arrhythmia

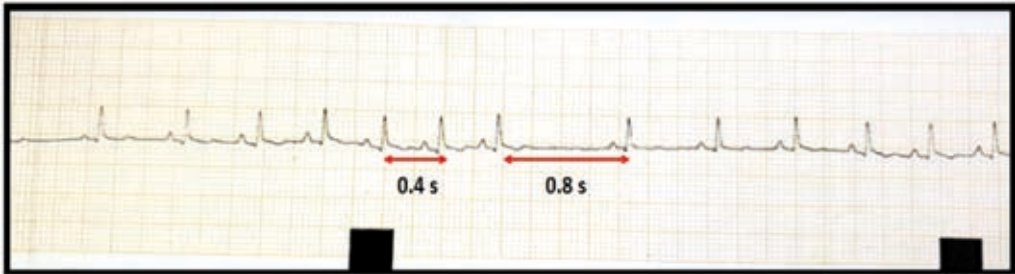


Fig. 2. Lead II, sensitivity 10mm/mV, speed 25mm/s, Sinus block



Fig. 3. Lead II, sensitivity 10mm/mV, speed 25mm/s, Elevated T wave

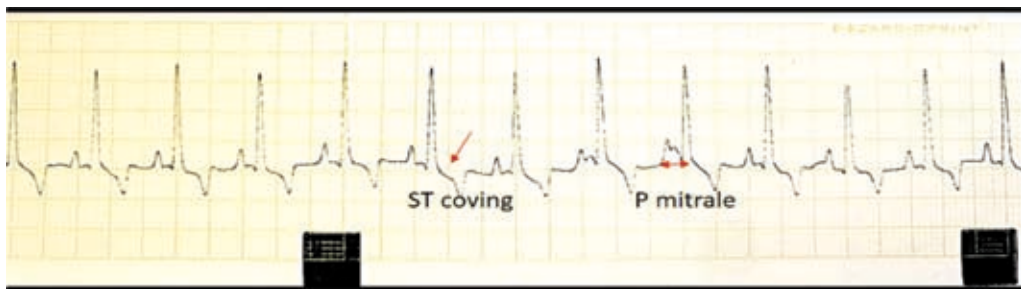


Fig. 4. Lead II, sensitivity 10mm/mV, speed 25mm/s, ST coving and P-mitrale

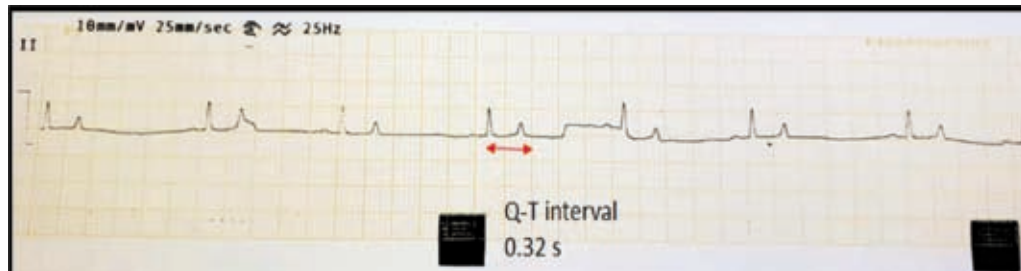


Fig. 5. Lead II, sensitivity 10mm/mV, speed 25mm/s, Prolonged QT interval and Low R amplitude

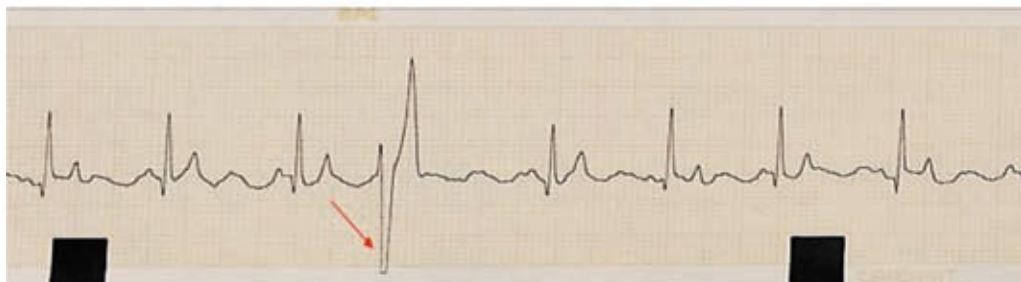


Fig. 6. Lead II, sensitivity 10mm/mv, speed 25mm/s, VPC (arrow)

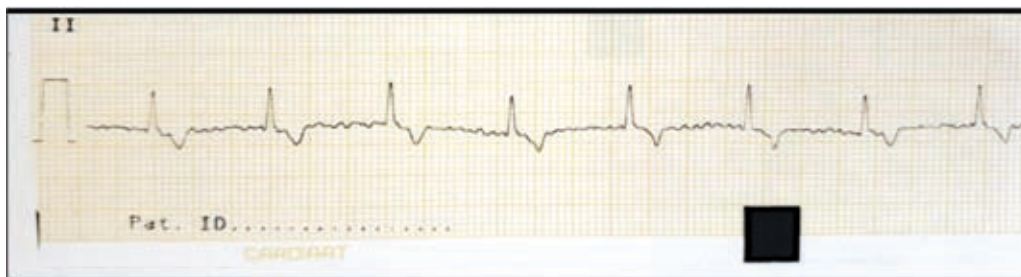


Fig. 7. Lead II, sensitivity 10mm/mV, speed 25mm/s, Atrial fibrillation

a compromised autonomic control would be present (Rubinger *et al.*, 2004) and this might be the reason for the variation in the RR interval.

Haematology

The mean values of haematological parameters are depicted in Table 2. Statistically, a significant increase in WBC, neutrophils and a decrease in RBC, haemoglobin and VPRC

were noticed. Increased levels of leucocytes might affect the electrical stability of the heart and progress into the development of congestive heart failure as suggested by Madjid *et al.* (2004). Neutrophilic leukocytosis reported in renal diseases might be associated with cellular damage, inflammatory changes, and cytokine release (Anjaly *et al.*, 2021). A significant decrease in RBC, haemoglobin and

VPRC might be due to the lack of erythropoiesis, gastrointestinal blood loss and reduced blood cell survival due to uraemia (Perini-Perera *et al.*, 2021). Anaemia in CKD would result in arrhythmia due to volume overload and decreased cardiac tissue oxygenation (Pouchelon *et al.*, 2015).

due to the reduced glomerular filtration rate (GFR) and decreased excretion of magnesium (de Lima *et al.*, 2022). It might lead to AV nodal and intraventricular conduction disturbances that might result in complete heart block and cardiac arrest (Bagshaw *et al.*, 2013).

Table 2. Mean values of haematological parameters of dogs with renal diseases

Sl. No	Parameters	Control (n=10)	Diseased group (n=20)	t-value	p-value
1	White blood cell count ($10^3/\mu\text{L}$)	12.15 ± 1.21	27.13 ± 4.98	2.09*	0.04
2	Neutrophils ($10^3/\mu\text{L}$)	9.29 ± 0.98	23.01 ± 4.59	2.08*	0.04
3	Lymphocytes ($10^3/\mu\text{L}$)	1.59 ± 0.18	2.42 ± 0.46	1.22	0.23
4	Monocytes ($10^3/\mu\text{L}$)	0.71 ± 0.16	1.43 ± 0.29	1.63	0.11
5	Red blood cell count ($10^6/\mu\text{L}$)	6.37 ± 0.30	4.65 ± 0.43	2.66*	0.01
6	Haemoglobin (g/dL)	15.34 ± 0.52	9.92 ± 0.80	4.52**	<0.001
7	Volume of packed red cells (per cent)	43.72 ± 1.88	29.16 ± 2.68	3.61**	<0.001
8	Platelet count ($\times 10^3/\mu\text{L}$)	277.8 ± 27.25	285.5 ± 35.96	0.14	0.89

*Significant at 0.05 level and ** Significant at 0.01 level

Serum- biochemical

The mean values of serum-biochemical parameters are depicted in Table 3. Statistically, a significant increase in magnesium, creatinine and BUN were noticed as compared to the control group. Loss of functional nephrons and diminished renal

Correlation studies

Correlation coefficients between haemato-biochemical and ECG parameters are given in Tables 4 and 5. A positive correlation exists between the RBC, haemoglobin, and VPRC with T amplitude and a negative correlation was presented between RBC,

Table 3. Mean values of Serum-biochemical parameters of dogs with renal diseases

Sl. No	Parameters	Control (n=10)	Diseased group (n=20)	t-value	p-value
1	Potassium (mmol/L)	4.65 ± 0.08	4.88 ± 0.28	0.54	0.58
2	Calcium (mg/dL)	9.41 ± 0.15	9.07 ± 0.46	0.50	0.61
3	Magnesium (mg/dL)	2.23 ± 0.13	3.11 ± 0.21	2.85 **	0.008
4	Creatinine (mg/dL)	0.91 ± 0.09	8.37 ± 1.39	3.73**	<0.001
5	Blood urea nitrogen (mg/dL)	19.46 ± 2.55	79.41 ± 6.82	6.06**	<0.001
6	Creatine kinase-MB (IU/L)	10.53 ± 1.07	10.30 ± 3.02	0.05	0.95
7	Alkaline phosphatase (IU/L)	126.3 ± 12.27	234.7 ± 56.05	1.35	0.18
8	Alanine transaminase (IU/L)	58.98 ± 6.29	65.27 ± 6.45	0.61	0.54

*Significant at 0.05 level and ** Significant at 0.01 level

excretion were the probable reasons for the elevated BUN, creatinine and magnesium (Sonu *et al.*, 2019). In end-stage renal failure uremic anorexia, hypodipsia and emesis would result in volume depletion and decreased cardiac output (Pouchelon *et al.*, 2015). The higher incidence of hypermagnesemia was probably

haemoglobin and VPRC with corrected QT interval. The anaemia associated with renal diseases would decrease T amplitude and prolong the corrected QT interval. It might be due to tissue hypoxia and restricted oxygen transport in the myocardium (Scheller *et al.*, 2011).

Table 4. Correlation coefficients between haematological and ECG parameters

	Rate	P amplitude	P duration	R amplitude	QRS duration	T amplitude	T duration	PR interval	QT interval	RR interval
WBC	0.30	0.21	-0.02	0.23	-0.09	-0.25	-0.21	-0.29	-0.49*	-0.19
Neutrophils	0.30	-0.23	-0.02	0.23	-0.11	-0.25	-0.25	-0.29	-0.46*	-0.19
Lymphocyte	0.36	0.14	-0.02	0.25	0.11	-0.00	0.26	-0.29	-0.62*	-0.32
Monocytes	-0.18	-0.16	0.17	0.01	-0.07	-0.26	0.06	0.15	-0.09	0.22
RBC	-0.25	0.15	0.14	0.04	-0.37	0.53*	0.03	-0.08	-0.61*	0.16
Haemoglobin	-0.20	0.10	0.02	0.04	-0.40	0.55*	0.05	-0.09	-0.56*	0.11
VPRC	-0.26	0.08	0.06	0.01	-0.40	0.56*	0.03	-0.15	-0.58*	0.17
Platelets	-0.16	-0.05	0.28	0.15	0.21	0.13	0.09	0.01	0.58*	0.10

*Significant at 0.05 level and ** Significant at 0.01 level

Table 5. Correlation coefficients between biochemical and ECG parameters

	Rate	P amplitude	P duration	R amplitude	QRS duration	T amplitude	T duration	PR interval	QT interval	RR interval
Potassium	0.002	-0.10	-0.05	0.04	0.27	0.37	0.15	0.04	0.24	-0.02
Calcium	0.2	0.24	-0.06	0.39	0.33	0.03	0.35	0.09	-0.37	-0.08
Magnesium	-0.46*	0.06	-0.04	0.06	0.14	0.33	0.48*	0.34	0.17	0.29
CK-MB	-0.32	-0.17	0.26	-0.05	-0.25	0.14	-0.14	-0.26	-0.05	0.26
Creatinine	-0.4	-0.24	-0.001	-0.56*	-0.19	-0.12	-0.17	0.4	0.62*	0.25
BUN	-0.2	0.01	-0.02	-0.09	0.04	-0.13	-0.01	0.29	0.78*	0.06
ALP	0.24	-0.03	-0.01	-0.2	0.28	0.04	-0.22	-0.17	-0.21	-0.22
ALT	-0.47*	0.2	0.43	0.17	-0.0003	0.44*	0.20	0.13	-0.10	0.32

*Significant at 0.05 level and ** Significant at 0.01 level

A positive correlation was noticed between creatinine and corrected QT interval, BUN, and corrected QT interval. The prolongation of QT interval might be used as a marker of susceptibility to ventricular arrhythmia and to assess electrolyte disturbances in canine renal diseases (Alfonso *et al.*, 2020). The negative correlation between creatinine and R amplitude was in accordance with Ravi *et al.* (2018) and this might be associated with uremic pericarditis.

A negative correlation obtained between WBC, neutrophils and lymphocytes with corrected QT interval was contradictory to the findings of Lazzerini *et al.* (2015) who suggested a prolongation of QT interval in inflammatory conditions. Magnesium was negatively correlated with heart rate. Increased magnesium in CKD resulted in conduction delay and hence a decrease in heart rate as suggested by Bagshaw *et al.* (2013).

Conclusion

Arrhythmia was more predominant

in animals with chronic kidney disease (CKD) followed by acute kidney injury (AKI). Sinus arrhythmia followed by first-degree AV block and wandering pacemaker were the common arrhythmia observed. A significant increase in R-R interval and a decrease in heart rate was noticed. The haemato-biochemical analysis revealed anaemia, leukocytosis with neutrophilia, elevated blood urea nitrogen (BUN) and creatinine level. A significant positive correlation was noticed between haemoglobin, volume of packed red cells (VPRC) and red blood cell count (RBC) with T amplitude and creatinine and BUN with corrected Q-T interval. A significant negative correlation was noticed between VPRC, RBC and haemoglobin with the corrected QT interval.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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