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PROGNOSTIC VALUE OF CARDIAC BIOMARKER AND ELECTRO-CARDIOGRAPHY OF CANINE PARVOVIRUS-2 AFFECTED KANNI PUPS: A STUDY OF EIGHT CASES

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Canine Parvovirus strains 2a, 2b, and 2c cause myocarditis and acute hemorrhagic gastroenteritis in dogs (Goddard and Leisewitz, 2010). Severe clinical condition mostly affects puppies of ≤ 6 months ages while adult dogs with immunological deficiencies are also at danger (Mylokanis *et al.,* 2016). The enteritis variant of myocarditis is less prevalent than the myocarditis form. This type of infection causes peracute mortality due to the heart failure in puppies infected during prenatal life or in infants younger than 8 weeks age whose moms are not vaccinated. Cardiac biomarkers are used as useful indicators for heart disease diagnosis. Such biomarkers include cardiac troponins (cTnI, cTnT), creatine kinase myocardial band (CK-MB), and brain natriuretic peptide (BNP) (Er and Ok, 2015). Cardiac troponins are reliable indicators of cardiac damage, and even minor elevations in these markers are significant in myocardial injury. In dogs with parvoviral enteritis large increases in blood CK-MB and BNP levels, as well as a modest rise in cTnI levels have been reported. Moreover, the evidences of hypercoagulability without disseminated intravascular coagulopathy have been documented in puppies with CPV enteritis (Otto *et al.,* 2000). In puppies with CPV enteritis, hypercoagulability without disseminated intravascular coagulopathy has been observed (Otto *et al.*, 2000). Robinson *et al.* (1979) have reported that viral myocarditis suspected puppies had small R waves, S-T segment elevation, QRS notching and paroxysmal ventricular tachycardia. Only very young cardiac muscle fiber (in puppies of <8 weeks age) was found susceptible to fatal parvoviral infection and had smaller R wave, ST segment elevation and QRS notching (Carpenter *et al.,* 1980). The aim of this study was to assess the changes in some selected cardiac biomarker such as cTnI, ECG changes and coagulation profiles in parvoviral enteritis and present the importance of these parameters for prognosis of the disease. Further, the study aimed to determine the presence of myocarditis in enteritis form of disease via cardiac biomarkers.

The present study was conducted at the Small Animal Medicine Unit of Veterinary Clinical Complex, Veterinary College and Research Institute, Orathanadu (India). Eight apparently healthy dogs with normal vital signs were taken as control group. Native Kanni breed pups of age 2 to 8 months with the history and clinical manifestations of canine parvo viral (CPV) enteritis, were selected after confirmation by PCR analysis. The diagnosis of CPV was performed by a PCR method (Ozkul *et al.,* 2002). Blood samples with and without anti-coagulant (sodium citrate) were collected from the pups affected with parvoviral enteritis and healthy dogs; and the plasma and serums were separated. The samples for evaluation of coagulation profiles and cardiac biomarkers were kept in a deep freezer until use. Cardiac troponin I was measured by using dry chemical cartridges in Abbott I-STAThand held machine. Prothrombin (PT) and activated partial prothrombin test (APTT) were measured by using Misfa clog automated coagulation profile machine (Agappe Diagnostic Ltd, India). Electrocardiographic recordings were made with standard electrocardiographic lead systems as per Tilley and Lawrence (1992) using BPL CardiartGenX 3 machine. Lead II was used to interpret electrocardiogram variables and compared with standard dog ECG for analysis.

Canine parvovirus enteritis is probably one of the most common infectious disorders of dogs and the most prevalent virus in dogs with infectious diarrhea. This highly contagious disease is caused by strains of CPV-2 (2, 2a, 2b, and 2c) (Craigand Nicola, 2012). CPV-2 spreads rapidly among dogs via faecal-oral route (direct transmission) or through oro-nasal exposure to fomites contaminated by faeces (indirect transmission) [Schoeman *et al.*, 2013]. The cardinal clinical signs in puppies with CPV were anorexia, lethargy, bloody diarrhea, vomiting, moderate or severe dehydration, tachycardia, hypothermia. Of the 8 puppies, 6 survived and one each died on 1st and 2nd day after initial treatment. The diagnosis of parvoviral enteritis in these dogs was established after PCR test were detected positive (Fig. 1). Acute hemorrhagic enteritis is the most common form. The myocarditis form is less common than enteritis form. This form causes per acute death due to heart failure in puppies infected in fetal life or as infants younger than 8 weeks age whose dams were not vaccinated (Hoskins, 1997). This might be the reason for the mortality of pup in our study.

Fig. 1: Diagnosis of CPV with a PCR

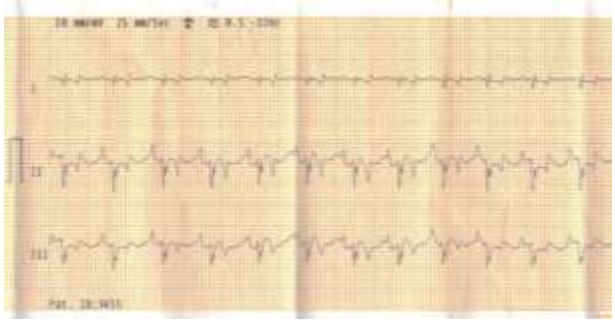

Fig. 2: Electrocardiogram of CPV-affected Kanni pup

Mean prothrombin time and activated partial prothrombin time in dogs with CPV enteritis was 5.5 ± 0.2 and 7.29 ± 0.4 sec, respectively, which was compared with control groups such as 7.89 ± 0.1 and 11.43 ± 0.01 sec, respectively. This study showed hypercoagulability of CPV affected dogs. Our results are in line with Cynthia and Scott (2000) who found dogs with CPV enteritis had high prevalence of clinical thrombosis or phlebitis and laboratory evidence of hypercoagulability without disseminated intravascular coagulopathy. It is thought to be due to an endotoxin- or cytokine-mediated procoagulant effect on endothelial cells. Loss of antithrombin through gastrointestinal tract, consumption of antithrombin as a result of endotoxin-mediated activation of coagulation, and hyper-fibrinogenaemia can contribute to hypercoagulable state seen in CPV enteritis (Otto *et al*., 2000).

A 'biomarker' is broadly defined as an indicator of a biological state that is objectively measured and evaluated as a marker of physiological or pathological processes. In canine parvovirus (CPV) infection these biomarkers could assist in increasing the index of suspicion for the disease. Troponin is the most commonly used biomarker in the diagnosis of acute myocardial damage (Apple, 1999). Troponin-I is considered a reliable serum biomarker for myocardial ischemia and necrosis in human and animals. After acute myocardial injury, cTnI is released from the cytoplasmic pool, resulting in increased blood concentrations within 2 h, with a peak after 12-24 h (DeClue *et al.*, 2011). Burgener *et al.* (2012) showed that cTnI level significantly increased in 24 to 48 h and then returned to basal level. Bastan *et al.* (2013) found that increased serum cTnI levels were consistent with short survival time in dogs with CPV-2. In present study, the mean cTnI value in CPV affected pups was 0.68 ± 0.23 ng dL^{-1}; whereas in control

Table 1: Parameters showing control and CPV affected dogs

Variables	Control group (n = 8)	Affected group (n = 8)
Pamp (mV)	0.185 ± 0.01	0.18 ± 0.01
P duration (sec)	0.04 ± 0.01	0.03 ± 0.12
QRS amp (mV)	1.82 ± 0.13	1.31 ± 0.02
QRS duration (sec)	0.04 ± 0.02	0.03 ± 0.001
PR interval (sec)	0.12 ± 0.02	0.12 ± 0.003
QT interval (sec)	0.22 ± 0.03	0.18 ± 0.06
T amp (mV)	0.25 ± 0.01	0.30 ± 0.01

dogs cTnI value was nil. The normal range of cTnI is 0.03-0.07 ng mL^{-1} (Sleeper *et al.,* 2001). The results in this study were higher than the normal physiological ranges reported in control dogs indicating myocardial injury. One of the pups showed cTnI value of 2.75 ng dL^{-1} on the day of admission and very next day pup succumbed to death. This might be due to acute myocardial injury in pup due to CPV.

Electrocardiography, a non-invasive and relatively inexpensive technique, is now accepted as an important diagnostic tool in detecting cardiac abnormalities in dogs (Tilley, 2008). It detects not only the disturbances of cardiac rate and rhythm, but also cardiac enlargement, myocardial disease, ischaemia, pericardial diseases, and certain electrolyte imbalances (Moneesh *et al.,* 2018). The ECG changes were documented in a study in which decrease in heart frequency values of the parvoviralenteritis affected dogs when compared to normal dogs was reported (Sravanthi *et al.,* 2019). Changes in QRS complexes of the infected animals were in terms of duration were noticed, low voltage QRS amplitude and QRS notching was also noted. This is an important consideration during clinical evaluation, as several leads with notched QRS complexes in dogs may indicate that a more thorough diagnostic examination is required. Myocardial dysfunction one of the most important consequences of sepsis in dogs (Otto *et al.,* 2000) and Small QRS wave was seen in CPV dogs with sub-acute myocarditis. The small number of dogs was a limiting factor in the study reported here, but the findings were important and in accordance with thrombosis in dogs with CPV enteritis. Although we cannot define the primary mechanism, results of our study suggest that reduction in AT activity are likely to contribute to early development of hypercoagulability in dogs with CPV enteritis. In conclusion, prolonged PT and aPTT, changes in ECG and increase in cardiac troponin levels were detected in parvoviral enteritis infection. It is concluded that acute myocarditis form may develop in the enteric form of the disease, based on ECG changes and troponin elevation.

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