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A Retrospective Analysis of Dilated Cardiomyopathy in Labrador Retrievers

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ABSTRACT

The present study was conducted to record the incidence, clinical presentation, electrocardiographic, radiographic, laboratory, two dimensional echocardiography, M-mode echocardiography, pulsed wave Doppler and color flow Doppler findings in Labrador Retrievers with Dilated Cardiomyopathy (DCM) for a period of five years from 2013 to 2018. It included 210 healthy dogs and 327 confirmed cases of DCM. The incidence of dilated cardiomyopathy in Labrador Retrievers was found to be 7.49 per cent in the present study. On radiography, cardiomegaly and pulmonary edema were the major findings observed. In echocardiography, increased left ventricular end diastolic dimension and systolic dimension, reduced fraction shortening, increased E-point sepal separation, increased Left atrium (LA) / Aorta (AO) ratio, decreased ejection fraction, increased end diastolic volume and end systolic volume were noticed. On pulsed wave Doppler echocardiography reduced pulmonary artery (PA), Aorta (AO), left ventricular outflow tract (LVOT), right ventricular outflow tract (RVOT) velocities were recorded. Mild to moderate regurgitation was observed in Mitral and Tricuspid valve by color flow Doppler echocardiography. M-mode derived chamber dimensions, E-point septal separation, ejection fraction, fractional shortening were reliable parameters in diagnosing Dilated Cardiomyopathy in Labrador Retrievers. Pulsed wave Doppler and color flow Doppler were useful in assessing velocity and flow pattern across valves.

Keywords: Dilated cardiomyopathy, Labrador Retrievers, Echocardiography

Idiopathic dilated cardiomyopathy (DCM) is a cardiac muscle disease of unknown origin characterized by enlargement of the cardiac chambers and severe systolic dysfunction (Ricahrdson *et al.,* 2006). It is a condition of unknown etiology characterized by a progressive dilatation of one or both ventricles with severe impairment of systolic function in the absence of congenital, coronary arterial, hypertensive, vascular, pulmonary parenchymal, valvular, or other cardiovascular disorders (Dukes-McEwan *et al*., 2003). Canine DCM has long suspected to have a genetic basis and various modes of inheritance have been reported. Early detection provides the opportunity to initiate medical therapy, which may prolong clinical sign-free survival (O'Grady *et al.,* 2009; Summerfield *et al.,* 2012; Stephenson *et al.,* 2012; Vollmar and Fox, 2016; Wess *et al.,* 2017).

MATERIALS AND METHODS

Study was carried out at Madras Veterinary College Teaching Hospital, Tamil Nadu Veterinary Animal Sciences University (TANUVAS) comprised of healthy and DCM Labrador retriever dogs. In five year period (June 2013 to June 2018) the number of Labrador retriever attended Madras Veterinary College Teaching Hospital was 4365, out of which 327 dogs were diagnosed with dilated cardiomyopathy and were taken up for the study. For control group, 210 apparently healthy male and female Labrador retrievers aged between 4 and 8 years presented to the hospital for health check-up and vaccination were

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taken for the assessment of baseline referral values of selected parameters. The study consisted of two groups which included apparently healthy Labrador Retrievers (Group I) and clinical cases of Dilated Cardiomyopathy (Group II). All the animals were subjected to Physical examination, laboratory investigation, radiography, electrocardiography, Doppler blood pressure and echocardiography. Laboratory investigation (haematology and biochemical) were conducted as per standard protocol using auto analyzer. The animals under study were subjected to thoracic radiography to record the changes and Vertebral Heart Score (Figure-1) was calculated (Jepsen – Grant *et al*., 2013). Electrocardiography (Dukes-McEwan *et al*., 2003) and systolic blood pressure was recorded as per the standard procedure (Crowe and Spreng, 1995).

Echocardiography

Echocardiographic examinations were performed as suggested by (Boon 2011) using ALOKA SSD 3500 ultra sound system with a cardiac probe of 3.0 – 6.0 MHz to obtain Two dimensional, M- mode, Pulsed wave and color flow Doppler echocardiography images of heart.

All dogs underwent complete echocardiographic examination, including transthoracic, 2-dimensional, M-mode, spectral, and color flow Doppler echocardiography. Examinations were performed in conscious unsedated dogs. Right parasternal M- mode recordings were obtained from short-axis views with the dogs positioned in right lateral recumbency, and the 2-dimensional echocardiograms were obtained in accordance with techniques described by Boon (2011). M-mode measurements were obtained according to the leading edge–to–leading edge method (Dukes-McEwan *et al*., 2003). M-mode images were obtained from the real time left ventricular transverse plane by placing the cursor over the structures. The resulting M-mode imaging as depth through the heart on the Y- axis and time on the X – axis and the following measurements were collected: E-point septal separation, Left ventricular diameter at end diastole (LVIDd), left ventricular diameter at end-systole (LVIDs), left ventricular posterior wall thickness at end- diastole (LVPWd), left ventricular posterior wall thickness at end-systole (LVPWs), interventricular septal thickness at end-diastole (IVSd) and interventricular septal thickness at end-systole (IVSs). From these above values the contraction indices like fraction shortening, interventricular septum fraction thickening and left ventricular posterior wall fraction thickening were calculated using the following formulas (Koch *et al.,* 1996). Fractional shortening = [(LVIDd – LVIDs)- LVIDd] × 100%, Interventricular septum fraction thickening = [(IVSs – IVSd) – IVSd] × 100% and Left ventricular posterior wall fraction thickening = [(LVPWs – LWPd)/ LWPd] × 100%. The left atrial–aortic root ratio (LA/Ao) was obtained from the 2-dimensional short-axis view (Hansson *et al. 2002)*. Ejection Fraction was calculated from Simpson's method of Disc (SMOD) derived end-diastolic and end-systolic LV volumes by using the following formula: Ejection Fraction = [(EDV – ESV)/EDV] × 100 % (Boon, 2011). Left ventricular EFs were obtained from whichever view optimizes left ventricular length and volume (right parasternal long-axis or left apical views) and was calculated by the area length method.

The spectral Doppler echocardiography and Color flow echocardiography was performed as described by Dukes-McEwan *et al*. (2003).

RESULTS AND DISCUSSION

Incidence

During the study period (June 2013 to June 2018) the total no of Labrador retrievers were brought to Madras Veterinary college teaching hospital for various reasons was 4365. In this 327 Labrador retrievers were diagnosed to have dilated cardiomyopathy accounting for prevalence of 7.49 per cent. The average age of affected dogs was 5.71 ± 0.11 years, and the incidence in male dogs were 69.72 per cent (228) and female dogs were 28.44 per cent (99). In the present study the prevalence of DCM in Labrador retrievers was found to be 7.49 per cent with male predominance. The average age of the affected dog was 5.71 ± 0.11 years. Grady and Sullivan (2004) reported 0.3 per cent incidence of DCM in Labrador retrievers from the University of Purdue Veterinary Medical Database 1985 to 1991. The present finding is not in agreement with Grady and Sullivan (2004). This higher prevalence of DCM in Labrador retrievers in this study may be due to the mode of inheritance in the ancestral population. McEwan (2000) opined that in the most of the familial DCM, autosomal dominant mode of inheritance was

suspected, whereas Ortiz-Lopez *et al.* (1996) considered autosomal dominant, autosomal recessive, X-linked and mitochondrial modes of inheritance in the DCM affected dogs. Therefore the ancestral population would have been heterozygotes or homozygotes for DCM related inheritance. Even very high incidence of around 24 per cent was observed by Vollmar (2019) in Irish wolfhounds. This gives a logical conclusion that the prevalence rate depends on the population under study.

In the present study the average age of DCM affected dogs was 5.71 ± 0.11 years years. This concurs with the findings of Dukes-McEwan *et al*. (2003) where they observed DCM at a mean age of 6.6 years. Tidholm and Jonsson (1996) in a study of Newfoundland dogs with DCM reported the mean age of affected dogs as 5 years which is less than the average of dogs affected with DCM in the present study. The incidence of DCM in male dogs was higher compared to females in the present study. This is in agreement with Tidholm and Jonsson (1996) who studied DCM in 37 Newfoundland dogs and reported 62 per cent in males and 38 per cent in females.

The major history and clinical signs were abdominal distension in 80.12 per cent of dogs, exercise intolerance in 70 per cent of dogs, weight loss in 70 per cent of dogs, cough in 60.24 per cent of dogs, episodic weakness in 19.5 per cent of dogs and syncope in 15.9 per cent of dogs. The above findings are in agreement with the study in 187 dogs with DCM by Tidholm *et al.* (1997).

The physical examination findings recorded were dyspnoea in 100 per cent of dogs, ascites in 97 per cent of dogs, gallop rhythm in 87 per cent of dogs, systolic murmur in 73 per cent of dogs, limb oedema in 53 per cent of dogs and weak femoral pulse in 50 per cent of dogs. These findings concur with several authors (Martin *et al.,* 2010). Dyspnoea may be due to pulmonary edema subsequent to left sided failure and ascites due to right sided failure. Systolic murmur and low pitched pro diastolic (S3) gallop sound was auscultated as an evidence of severe ventricular diastolic impairment (Martin *et al.,* 2010).

Highly significant increase in Blood urea nitrogen and Creatinine were noticed in DCM dogs compared to control. Significant decrease in the total protein and significant increase in the potassium were noticed authors Dukes-McEwan *et al*. (2003) and Martin *et al*. (2009) recorded elevated blood urea nitrogen and Creatinine, elevated liver enzymes and hypoprotenemia. But in the present study although significant change were observed in certain biochemical parameters they were within the normal ranges.

Highly significant increase in the mean ± S.E values of vertebral heart score was noticed in DCM dogs (11.87±0.054) compared to control (10.75 ± 0.06). The other major radiographic abnormalities in the DCM affected dog were cardiomegaly (Fig. 1) in 100 per cent of dogs, pulmonary edema in 80 per cent of dogs and pleural effusion in 20 per cent of dogs. These findings are in agreement with Dukes-McEwan *et al*. (2003) and Martin *et al*. (2010). Highly significant increase in the Vertebral Heart Score (11.87±0.054) was observed in DCM dogs compared to normal (10.75 ± 0.06). Lamb *et al*. (2001) recorded Vertebral Heart Score of 10.6 in health Labrador retrievers which concurs with the present study. No reports are available on Vertebral Heart Score of Labrador retrievers in DCM. This finding is in contrast with Jepsen –Grant *et al*. (2013) who opined that the observer's accuracy of diagnosis did not change significantly as a result of using vertebral heart score as an adjuvant to subjective assessment of radiography.

Normal sinus rhythm was appreciated in 63.3 per cent of dogs and ST depression in 70.03 per cent of dogs that were affected with DCM. The abnormal rhythm which includes Atrial fibrillation (Fig2) was present in 27.5 per cent of dogs, Ventricular premature contraction in 9.17 per cent of dogs. ST depression was consistently observed in 70.03 per cent of dogs with DCM as an indication of cardiomegaly. Major rhythm disturbances observed were AF in 27.5 per cent of dogs and VPC in 9.17 per cent of dogs. Majority of the dogs showed normal sinus rhythm. The findings in the present study is in agreement with several authors which includes Borgarelli *et al.* (2006), Dukes-McEwan *et al*. (2003) and Calvert and Wall (2001). They all observed Atrial fibrillation and Ventricular premature contraction as the common arrhythmias in dilated cardiomyopathy affected dogs across the breeds. However, no much change in the other quantitative parameters to assess the enlargement pattern was seen and also 63 per cent of dogs had normal sinus rhythm.

Echocardiography

Highly significant increase in the mean value of LA Ao,

LA/Ao (Fig 4), EDV and ESV and highly significant decrease in the ejection fraction were observed in DCM affected dogs compared to control (Table 1).

Table 1: Mean ± S.E of Two dimensional, M-mode, Pulsed wave Doppler echocardiography values in control and DCM dogs

Parameters	Control	DCM	T-value
	Mean ± S.E (n=210)	Mean ± S.E (n=327)	
LA cm	2.32±0.06	4.61±0.26	0.00**
Ao cm	2.23±0.08	2.01±0.16	0.00**
LA/Ao	1.04±0.01	2.41±0.21	0.00**
EDV ml	53.07±0.69	136.29±11.98	0.00**
ESV ml	24.98±0.38	95.92±10.2	0.00**
SVml	28.17±0.65	54.95±7.04	0.92 NS
EF (%)	52.85±0.77	36.11±3.716	0.00**
LVIDd cm	4.01±0.05	5.42±0.3	0.00**
LVIDs cm	2.66±0.07	4.67±.33	0.00**
RVIDd cm	0.96±0.05	1.28±0.12	0.01*
RVIDs cm	0.81±0.04	1.26±0.11	0.00**
IVSd cm	0.77±0.02	0.73±0.05	0.16 NS
IVS s cm	0.94±0.03	0.85±0.05	0.00**
LVPWd cm	0.91±0.04	0.78±0.02	0.06 NS
LVPWs cm	1.24±0.04	0.96±0.04	0.00**
FS%	34.66±0.88	14.46±2.43	0.00**
EPSS	0.81±0.01	1.94±0.13	0.00**
IVS FT%	27.22±1.59	15.99±2.23	0.00**
LVPW FT%	39.92±3.26	26.04±5.48	0.03*
LA Peak E-velocity (m/sec)	0.98±0.04	1.16±0.09	0.00**
RA Peak E-velocity (m/sec)	0.96±0.03	1.05±0.07	0.00**
Ao (m/sec)	1.19±0.02	0.79±0.03	0.00**
PA (m/sec)	0.97±0.01	0.55±0.04	0.00**
MV Peak E-velocity (m/sec)	1.04±0.03	1.16±0.07	0.04*
TV Peak E-velocity (m/sec)	0.92±0.03	1.14±0.04	0.00**
MV regurgitant velocity (m/sec)	Nil	3.04±0.027	Nil
TV regurgitant velocity (m/sec)	Nil	2.61 ±.022	Nil
LV OT (m/sec)	0.99±0.03	0.81±0.04	0.00**
RV OT (m/sec)	0.93±0.02	0.57±0.03	0.00**

These findings are in partial agreement with Borgarelli *et al.* (2006) in a study of 63 dogs with DCM reported EF as 27.7 per cent. McEwan *et al.* (2003) suggested that less than 40 per cent of EF determined by modified Simpson's rule was abnormally low. In the present study, DCM dogs showed an ejection fraction of 36.11±3.716 per cent when compared to 52.85±0.77 per cent in control dogs which is in agreement with the above study. The Simpson's method of disc (SMOD) method shows best correlation with actual left ventricular volume in the diseased heart and appears relatively unaffected by changes in the ventricular geometry (Borgarelli *et al.,* 2006). The present study involved SMOD for calculating EF. Therefore, reliability of this data is more, although several studies in dogs showed a high correlation between M-mode derived volumes and cardiac output by using Teicholz method in normal dogs, its reliability in diseased heart remains questionable because of the altered ventricular geometry.

Highly significant increase in the LVIDd, LVIDs, RVIDs (Fig. 3) and EPSS were noticed in DCM dogs compared to control given in Table 1. Significant increase in the values of RVIDd was noticed in DCM dogs compared to control. Highly significant decrease in the values of IVSs, LVPWs, FS and IVS FT were noticed in DCM dogs compared to control. Significant decrease in the values of LVPW FT was noticed in DCM dogs compared to control.

Tidholm and Jonsson (1996) in a study of 37 Newfoundland dogs with DCM recorded left ventricular hypo kinesis in 100 per cent of cases with FS ranging from 5 to 22 per cent, left ventricular end diastolic diameter (LVIDd) ranged from 5.0 to 8.4 cm and left ventricular end systolic diameter (LVIDs) ranged from 4.3 to 8.0 cm. This is in agreement with the present study. In the present study increased left ventricular dimensions in end diastole LVIDd, end systole LVIDs, thinning of interventricular septum and thinning of left ventricular posterior wall in diastole with reduced thickening of interventricular septum and left ventricular posterior wall during systole when compared with normal dogs (Table 1) were observed . These findings concur with Vollmar (2019) who in a study of DCM in Irish wolfhounds reported similar findings. The presence or absence of left ventricular volume overload is determined from diastolic dimensions. This measurement reflect maximum ventricular filling when the heart is relaxed. Systolic dimensions are a reflector of systolic function in a heart and should not be used to assess the presence

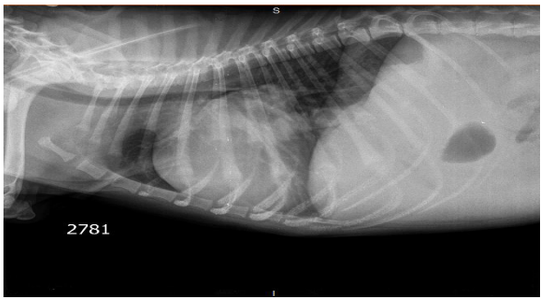

Fig. 1: Cardiomegaly in lateral radiography of DCM dogs

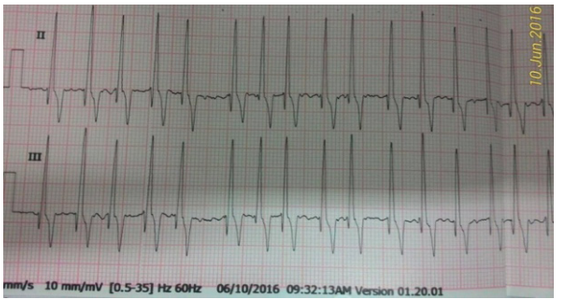

Fig. 2: Atrial fibrillation in DCM dogs

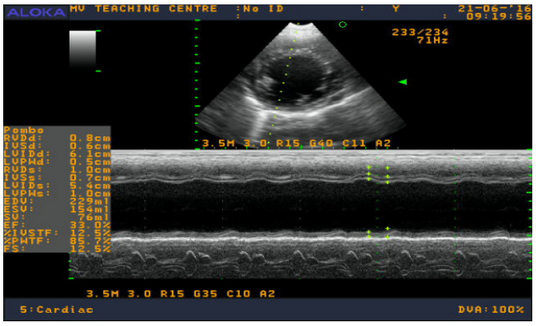

Fig. 3: M-mode measurements of left ventricle at the level of papillary muscle in DCM dogs

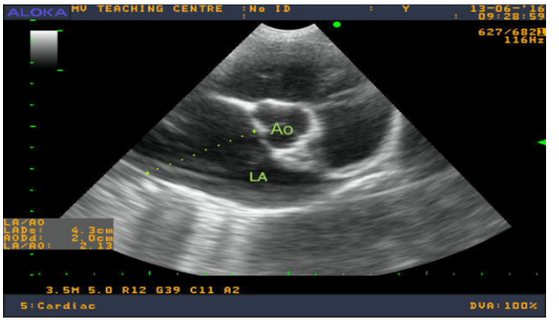

Fig. 4: Dilated left atrium at the right parasternal short axis view in DCM dogs

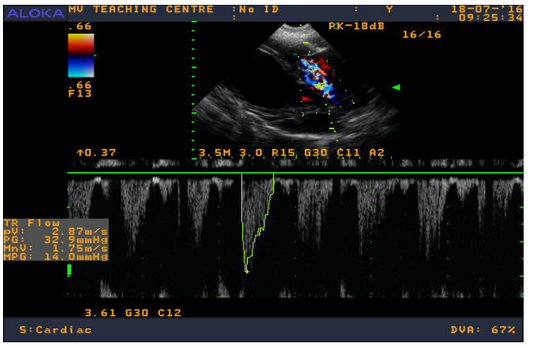

Fig. 5: Pulse wave doppler measurement of tricuspid valve (pulmonary hypertension) in DCM dogs

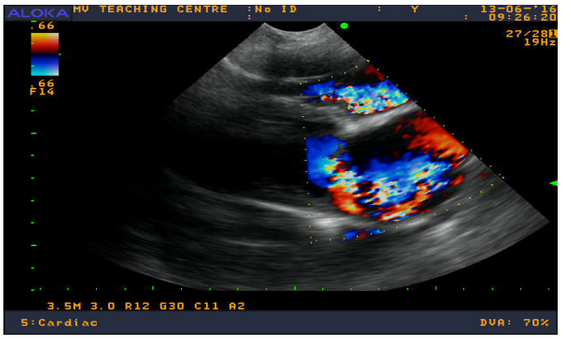

Fig. 6: Mitral and Tricuspid valve regurgitation in DCM dogs

or absence of dilation. The same principle applies to wall and septal thickness measurements. The presence or absence of hypertrophy can be determined from diastolic measurement of thickness. Systolic measurements of wall thickness are a reflection of systolic function so reduced thickness during systole may simply reflect decreased function (Boon, 2011).

Highly significant decreased in the fraction shortening was observed in DCM dogs compared to control. This findings is in agreement with (Dukes-McEwan *et al*., 2003, McEwan *et al.*, 2000; McEwan *et al*., 2003 and Borgarelli *et al.,* 2006, Dutton and Lopez-Alvarez, 2018, Vollmar, 2019). Kittleson (1998) categorized the severity of DCM based on M-mode derived fraction shortening as mild, moderate and severe therefore in the present study DCM can be categorized as severe since the mean FS was 14.46±2.43 per cent.

Tidholom and Jonsson (1996) in a study of 37 Newfoundland dogs with DCM recorded left ventricular hypo kinesis in 100 per cent of cases with FS ranging from

5 to 22 per cent which concurs with the present study. It is important to remember that fractional shortening is not a measure of contractility but is a measure of function. The three conditions that affect the fraction shortening the most are preload, afterload and contractility. Each one of these may individually or together affect the FS. When a low fractional shortening is calculated, it may be secondary to poor preload, increased after load or decreased contractility. To differentiate between these factors left ventricular end diastolic dimension measurement and blood pressure measurement are important. When increased left ventricular diastolic size is present and normal blood pressure is measured then reduced preload and increased afterload can be ruled out. Therefore measurement of blood pressure and LVIDd remains as a deciding factor to say that poor contractility is present.

In the present study there was highly significant increase in EPSS (1.94±0.13cm) in DCM dogs compared to control. This finding concurred with several authors (McEwan *et al.*, 2000; Dukes-McEwan *et al*., 2003; Dutton and Lopez-Alvarez, 2018; Vollmar, 2019). McEwan *et al*. (2003) and Borgarelli *et al.* (2006) opined that EPSS was a most sensitive and specific criteria for the recognition of early cardiomyopathy. McEwan *et al.* (2003) proposed increased mitral valve EPSS as one among the guidelines for the diagnosis of DCM.

Boon (2011) was of opinion that E-point to septal separation is one of the consistent and popular mitral and mitral insufficiencies. This correlation to ejection fraction is based on the fact that flow into the ventricle is equal to flow leaving ventricle. Therefore in DCM presence of high end diastolic left ventricular pressures reduce flow from left atrium to left ventricle due to reduced ventricular complaince and consequently flow out of left ventricle is also reduced. EPSS accurately separates normal from abnormal left ventricular function regardless of left ventricular size when dilatation is present. Hence EPSS is also valid for assessing left ventricular function in the presence of abnormal septal motion.

In the present study for mitral valve, tricuspid valve, LA and RA peak E-velocities were taken into account. This is because in normal animals, peak E-velocity represents rapid ventricular filling and peak A represents secondary atrial contractions. Where in DCM cases, rapid heart rate will cause two filling phases to overlap resulting in super imposed waveforms, this overlap will start to appear at heart rates approaching 125 beats per minute and complete loss of separation always will be present when the heart rate exceeds 200 beats per minute. In the present study the average heart rate was 176.25±7.54 bpm and therefore only the peak E-velocity were recorded.

Highly significant increase in tricuspid valve velocity (1.14±0.04m/sec), LA velocity (1.16±0.09m/sec) (Fig. 9), RA velocity (1.05±0.07m/sec) and significant increase in mitral valve velocity (1.16±0.07m/sec) were appreciated in the present study. The increased E-velocity may be secondary to increased atrial pressure or volume associated with insufficiency of the valves concerned.

The average regurgitant velocity recorded in the present study at mitral and tricuspid valves were 3.04±0.027 m/sec (Fig. 5) and 2.61 ±.022 m/sec respectively. This regurgitant velocity may be attributed to mild to moderate regurgitation at the valves because of the altered geometry of the ventricles due to dilatation and pulmonary hypertension (Kellihan and Stepien, 2010).

Highly significant decrease observed in the velocities of all out flow valves i.e. aorta (0.79±0.03 m/sec), pulmonary artery (0.55±0.04 m/sec), LVOT (0.81±0.04 m/sec), and RVOT (0.57±0.03 m/sec) were noticed in DCM dogs compared to control. These findings may be attributed to severe systolic failure in the DCM affected dogs.

In control group normal flow pattern was observed in LA, RA, Ao, PA, MV, TV, LV OT and RV OT. In DCM group no change in the flow pattern was observed across Ao and PA in any of the dogs, where as normal flow pattern across MV and TV were observed in only 33 per cent of dogs. Mitral valve regurgitation was noticed in 66.9 per cent of dogs which include mild regurgitation in 44.3 per cent of dogs and moderate regurgitation in 22.9 per cent of dogs. Tricuspid valve regurgitation (Fig. 6) was noticed in 40 per cent of dogs which include mild regurgitation in 22.9 per cent of dogs and moderate regurgitation in 17.12 per cent of dogs. Both mitral and tricuspid valve regurgitation was noticed in 40 per cent of dogs. In the present study only mild to moderate regurgitation was appreciated as the jet was occupying less than 50 per cent of the atrial area. This regurgitation may be attributed to abnormal dilation of the chambers leading to altered geometry and consequent leak in the AV valves and pulmonary hypertension, Boon (2011).

The higher prevalence of DCM was recorded in Labradors. Radiography was an important aid in assessing pulmonary edema and the Vertebral Heart Score serves as a screening test for Dilated cardiomyopathy. Two-dimensional echocardiography derived volumes and ejection fraction were found to be more reliable and M-mode derived chamber dimensions, E-point septal separation and fractional shortening remains as a gold standard for diagnosing Dilated Cardiomyopathy in Labrador retrievers.

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