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Clinical Study on Comparative Evaluation of Diagnostic Modalities in the Diagnosis of Hepatic Affections in Dogs

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ABSTRACT

A clinical study was conducted on 13 dogs including six apparently healthy dogs (Gp I) and seven dogs with symptoms of hepatobilliary involvement (Gp II) to evaluate different diagnostic modalities in making diagnosis. After recording signalment and history various hemato-biochemical parameters were estimated. Radiography and ultrasonography of liver was performed in all dogs. Thereafter, fine needle biopsy and histopathology were performed in Gp II dogs. The Hb and PCV were significantly low in Gp II as compared to Gp I whereas the TLC of Gp II was significantly higher than that of Gp I. The clotting time and bleeding time were significantly higher in Gp II as compared to Gp I. The ALT, AST and ALP values of Gp II were significantly higher than that of Gp I. The A:G ratio was significantly lower in Gp II as compared to that of Gp I. Sensitivity of radiography and ultrasonography were 57.14% and 100% and respectively. Accuracy of ultrasound guided biopsy was 100 % and different diseases diagnosed on histopathology were cholangiocellular carcinoma, liver cirrhosis, papillary adenocarcinoma, cystic adenocarcinoma, hemangiosarcoma and fibroadenoma. From the present study it was concluded that all the diagnostic modalities viz. laboratory tests, radiography and ultrasonography complimented each other in making diagnosis and predicting prognosis but the final diagnosis was obtained only with histopathology.

HIGHLIGHTS

- Ultrasonography has more sensitivity in detection of hepatic lesions
- Liver enzymes estimation is not specific to any disease but it helps in assessing the severity of the disease.
- The diagnosis was done on the basis of biochemical tests, radiography, ultrasonography and histopathology.

Keywords: Dog, Haematobiochemical, Liver, Radiography, Ultrasonography, Histopathology

Liver diseases in pets as well as people are very complex. The diagnosis of liver disorders is a challenge to clinicians because clinical signs are often very vague and non-specific, especially in the early stage of hepatobiliary diseases (Saravanan *et al.*, 2014). Because of varied functions of liver, no single test can accurately identify the hepatic disease or its underlying cause; hence a battery of tests is required to diagnose a hepatobiliary disorder. Although hemato-biochemistry is considered as an important preliminary tool for proceeding towards the correct diagnosis, radiography and ultrasonography

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are useful to evaluate the morphological abnormalities and liver parenchymal detail, respectively (Kumar *et al.*, 2012). Liver –specific serum enzyme activities are included routinely in screening serum biochemistry panel and are regarded as markers of hepatocellular and billiary injury and reactivity. Radiography, ultrasonography, and advanced imaging can be used for the diagnosis, staging, and surgical planning of cats and dogs with hepatobiliary tumors. Abdominal ultrasonography is the preferred method for identifying and characterizing hepatobiliary tumors in cats and dogs as radiographic findings are not specific for the diagnosis of a hepatic mass and do not provide information on the relationship of the hepatic mass with regional anatomic structures (Liptak *et al.*, 2004). Sonographic examination is useful in determining the presence of a hepatic mass and for defining the tumour as cystic or solid, and massive, nodular, or diffuse and this technique may also be used to obtain biopsy specimens from the liver tissue and masses adjacent to the liver. Ultrasonography helps to localize lesions larger than 0.5 cm in size and differentiating focal from diffuse disease and obstructive from non-obstructive icterus (Kumar *et al.*, 2012). Local extension and regional metastasis can be assessed with abdominal USG, CT, MRI, or laparoscopy. A tentative diagnosis of hepatic disease can be made by correlating the ultrasonographic abnormalities with the history, physical examination findings, laboratory tests and radiographic or laparoscopic observations. However to reach at a definitive diagnosis, liver biopsy and histopathology is usually required. Biopsy is a method which aids in determination of a precise diagnosis and disease prognosis (Rockey *et al.*, 2009). In clinical practice of dogs and cats diseases fine needle aspiration biopsy of the liver is most commonly performed (Wypij, 2011). Fine needle aspiration biopsy is a safe technique possible to perform even in out-patient clinic conditions (Suchocka *et al.*, 2013). With the increasing availability of ultrasound to the veterinarian, ultrasound guided biopsy techniques are used frequently Ultrasound-guided biopsies allow samples to be taken from a specific lesion, helping to avoid large vessels and biliary ducts and in most dogs, biopsy of the liver can be performed using local anaesthesia and minimal sedation. Literature describing individual diagnostic modality is sufficient, however, data regarding the comparison of various diagnostic moadalities in diagnosis of heaptic lesions is sparse. So the study was conducted to evaluate and compare different diagnostic modalities *viz.* laboratory tests, radiography, ultrasonography (B-mode and Doppler USG) and fine needle biopsy in the diagnosis of the hepatic affections in dogs.

MATERIALS AND METHODS

The study included six healthy dogs (Control, Gp I) brought to Teaching Veterinary Clinical Complex (TVCC) of SKUAST- Jammu for routine vaccination and seven dogs brought with history and clinical signs of hepatobilliary involvement (Gp II). After recording signalment and history various haematological parameters were determined using Mythic 18 vet, hematology analyzer. Differential leukocyte count was done by standard slide method. Clotting time (CT) and bleeding time (BT) were determined by capillary tube method and toe nail bleeding method, respectively. Various biochemical parameters were estimated using ERBA kits (Bayer Diagnostic Ltd., Baroda, India) on a chemistry analyzer (Chemistry analyser, RT 1904C KAYTO, Japan) and albumin globulin ratio (A:G) was calculated manually. Standard VD and lateral radiographs of cranial abdomen were taken using 500 mA Siemen (Heliopos-D) X-ray machine and processed on Carestream CR machine. The scanning of the liver was carried out using microconvex probe (D3C20L, 2.5-6.4 MHz) and linear probe (D7L40L, 5.0-10.0 MHz) of CHISON i8VET ultrasound machine. Ultrasound guided biopsies of hepatic lesions were obtained under local infiltration anaesthesia and histopathology was done to obtain the final diagnosis in Gp II dogs only. The data obtained from laboratory tests was analysed using one way ANOVA at 5% level of significance, using SPSS computer software.

RESULTS AND DISCUSSION

Signalment and symptoms

The average age and weight of Gp I dogs were 5.16 years (range 4-6 years) and 20.88 kg, respectively and included two Labradors, two non-descript dogs, one pug and one German shepherd dog. The average age and weight of dogs with hepatic affections (Gp II) was 7.3 years (range 1.5 to 12.5 years) and 28.7kg, respectively. Breeds affected were Labrador (n=2), German shepherd (n=2), Spitz (n=2) and Bull Mastiff (n=1). The results of the study revealed that hepatic affections can result in any breed

of any weight and at any age. The breeds affected were the commonly domesticated/reared breeds of this region. Mandigers *et al.* (2004) reported that liver disease was present between 4 and 6 years of age. Age predilection studies had documented that liver disorders generally occurred in higher frequency in dogs aged above 4 years (Sumathi *et al.*, 2017). They further reported that dogs aged 4 to 8 years had a higher incidence (36%) of liver disorders followed by dogs aged 8 years and above (34%). In present study four dogs were males and three were females. Earlier studies have reported no sex predilection in dogs for primary hepatobiliary tumors (Trigo *et al.*, 1982) and chronic hepatitis (Strombeck *et al.*, 1988). Samy *et al.* (2014) also reported that the breed, sex and weight did not play any role in the incidence of hepatic pathologies or surgical affections. However, Speeti *et al.* (1996) reported that females were more commonly affected with chronic hepatitis. In present study dogs with hepatic affections showed inappetance/anorexia ranging from 2 days to 1 month, intermittent vomiting, abdominal distension and depression. Kumar *et al.* (2012) reported similar signs in cases of hepatic neoplasia. Elhiblu *et al.* (2015) reported inappetance, halitosis, melena, hematochezia, polyuria, polydypsia, dehydration, icterus, weight loss and abdominal distension in cirrhotic dogs. Earlier studies reported that the potential findings in hepatobiliary neoplasia may include a cranial abdominal mass and hepatomegaly with hepatodynia, pallor, jaundice and cachexia (Johnson and Sherding, 1994; Nelson and Couto, 1998).

Laboratory tests

Various hemato-biochemical parameters recorded in Gp I and Gp II are presented in table 1 and 2, respectively. The Hemato-biochemical parameters of Gp I dogs were within normal physiological limits which indicated their healthy status. The values were similar to those reported by Kaneko *et al.* (2008), Morgan (2008), and Porter and Kaplan (2011).

The dogs of Gp II were anaemic. The mean haemoglobin and PCV values were significantly low in Gp II as compared to Gp I whereas the mean TLC value of Gp II was significantly higher than that of Gp I. The mean TEC value of Gp II was lower than that of Gp I, however the difference was not significant. The colour of mucus membrane was bright pink in Gp I dogs whereas it varied from pale to pink in Gp II. Findings of the study were similar to Washabau (2010); Saravanan *et al.* (2014) and Elhiblu *et al.* (2015). Sharma *et al.* (2001) reported that the liver dysfunction may lead to anaemia as liver being the prime organ involved in the production of erythropoietin and other factors required for erythropoiesis. The clotting time and bleeding time were significantly higher in Gp II as compared to Gp I which might be due to significantly lower concentrations of fibrinogen, protein C activity (Mischke *et al.*, 1998; Toulza *et al.*, 2006) and factors VII and X (Mischke *et al.*, 1998). Prins *et al.* (2010) reported that coagulation abnormalities were most severe in dogs with chronic hepatitis (CH) plus cirrhosis which showed significantly lower platelet counts, significantly

Table 1: Haematological parameters of Gp I and Gp II dogs

Gps	Hb (g/dl)	TLC ($x10^3$/µl)	Neutrophils (%)	Lymphocytes (%)	Others (M, E and B,%)	PCV (%)	TEC ($x10^6$/µL)	CT (sec)	BT (Min)
I (n=6)	12.55 ± 0.32^b	7.09 ± 0.30^a	66.62 ± 0.90	28.20 ± 0.59	5.18 ± 0.53	40.00 ± 1.19^b	5.06 ± 0.11	97.50 ± 6.42^a	3.83 ± 0.24^a
II (n=7)	8.04 ± 1.09^a	18.63 ± 2.59^b	72.40 ± 3.60	21.93 ± 3.12	6.10 ± 1.38	25.20 ± 3.59^a	3.983 ± 0.609	122.86 ± 6.34^b	4.71 ± 0.15^b

Mean±SEM values with different superscript differ significantly ($P<0.05$).

Table 2: Biochemical parameters of Gp I and Gp II dogs

GP	BUN (mg/dL)	CRTN (mg/dL)	ALT (U/L)	AST (U/L)	AP (U/L)	TP (g/dL)	ALB (g/dL)	A:G Ratio	TB (mg/dL)
I	16.56 ± 2.63	0.95 ± 0.14	15.17 ± 1.84^a	22.15 ± 3.99^a	33.60 ± 3.87^a	6.26 ± 0.21	3.68 ± 0.17	1.38 ± 0.12^b	0.49 ± 0.06
II	42.02 ± 21.43	2.38 ± 1.11	41.53 ± 8.59^b	42.65 ± 7.67^b	344.50 ± 93.18^b	6.64 ± 0.85	2.65 ± 0.46	$0.72^a \pm 0.11$	0.49 ± 0.16

Mean±SEM values with different superscript differ significantly ($P<0.05$).

prolonged activated partial thromboplastin time (APTT), significantly lower factor IX activity and significantly lower anti-thrombin (AT). Decreased synthesis rather than consumption of factors was thought to be the cause of the coagulation abnormalities.

The ALT, AST and ALP values of Gp II were significantly higher than that of Gp I. However, the values of ALT and AST were within physiological limits but the value of ALP was higher than the upper physiological limit. These findings were concurrent with the earlier studies (Saravanan, 2014; Elhiblu *et al.*, 2015). Font *et al.* (1989) also reported normal hepatic enzyme levels in liver cirrhosis. High ALP could indicate primary hepatic disease; however, in dogs ALP is not liver specific and its elevation may be due to extrahepatic sources. Marked ALP increases were noticed in dogs with mammary tumours and other neoplasms (Center, 1996; Leveille-Webster, 2000). Tennant and Center (2008) reported that serum ALT and AST measurements were highly useful in detecting hepatocellular injury and monitoring clinical progress. Solter *et al.* (1994) reported high serum ALP as a sensitive marker for cholestasis in most of the mammalian species including dogs. In present study there was no significant difference in BUN, CRTN, TP, Albumin and total bilirubin values between the two groups, however the BUN and CRTN values were slightly higher in Gp II. The A:G ratio was significantly lower in Gp II as compared to that of Gp I. The role of liver in the synthesis of major plasma protein as well as the site of degradation and synthesis of many other proteins could be the cause of decreased albumin concentration and decreased A:G ratio (Webster, 2005). Moreover, ascites leads to increased albumin distribution and lower blood albumin concentration, which decrease the plasma oncotic pressure and aggravates the ascites.

Radiography

The liver was visible in all the six dogs of Gp I in lateral as well as VD radiographs. The liver had soft tissue opacity and was visible within the intrathoracic portion of abdominal cavity on lateral and VD views; however, gall bladder was not visible in any dog in any view. Kumar *et al.* (2012) reported that survey abdominal radiographs are useful to evaluate the morphological abnormalities in size, shape, position and density (mineralisation/radiolucencies) of the liver and presence of abdominal effusion. However, lack of abdominal contrast and insensitivity to detect subtle changes limits the precision of abdominal radiography. Popesko *et al.* (1990) reported that the liver image considerably beyond the rib arch may be considered to be liver enlargement. However, Partington and Biller (1995) reported that radiographic evaluation of alteration in liver size is somewhat subjective and insensitive to subtle changes.

Out of seven animals of Gp II, hepatic lesion was identified radiographically in four (57.14%) dogs only, while in remaining three dogs ascites masked the details of abdominal organs. Major radiographic findings recorded in the animals with hepatic affections were ground glass appearance of abdominal cavity in cases of ascites (n=3) (Fig. 1), mid abdominal soft tissue opacity pushing all intestines caudally (n=5) (Fig. 2), extension of liver lobes well beyond rib cage indicating hepatomegaly (n=2) (Fig. 3) and increased opacity of liver (n=3) (Fig. 4) on lateral radiographs.

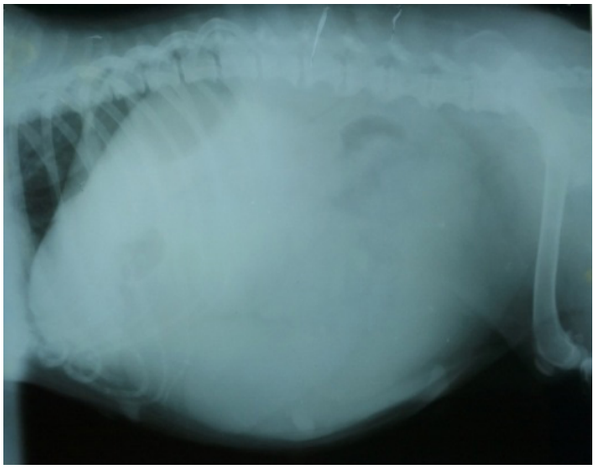

Fig. 1: Lateral view of abdomen of a dog with hepatic cirrhosis showing abdominal distension with ground glass appearance, loss of serosal details indicating ascites

However, the radiographic lesions were not specific for any disease. Similar radiographic findings were reported by Kumar *et al.* (2012) in dogs with hepatic lesions. Suter (1982) reported that hepatomegaly is reliable radiographic sign of liver disease which may be diffuse, with uniform enlargement of all lobes or focal, with enlargement of only a single lobe.

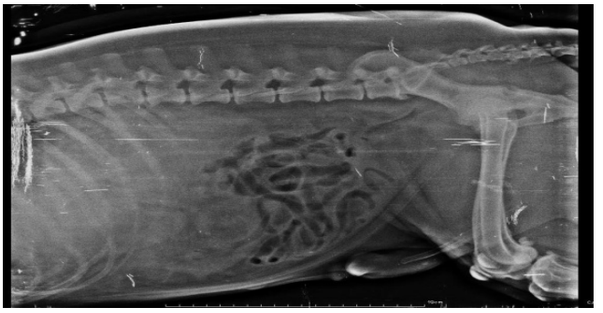

Fig. 2: Lateral view of abdomen of a dog with papillary adenocarcinoma showing an irregular soft tissue mass in the cranial abdomen extending beyond the umbilicus and pushing stomach, spleen and intestines caudally

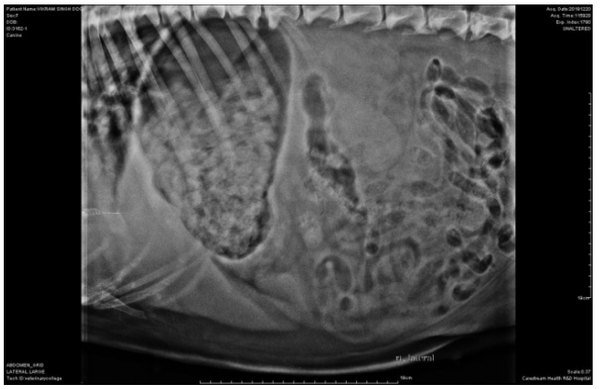

Fig. 3: Left lateral view of abdominal of a dog with collangiocellular carcinoma showing hepatic enlargement indicated by left lateral lobe extending far beyond the costal arch and soft tissue opacity caudal to the stomach displacing the stomach, spleen, kidneys caudally and intestines ventrally

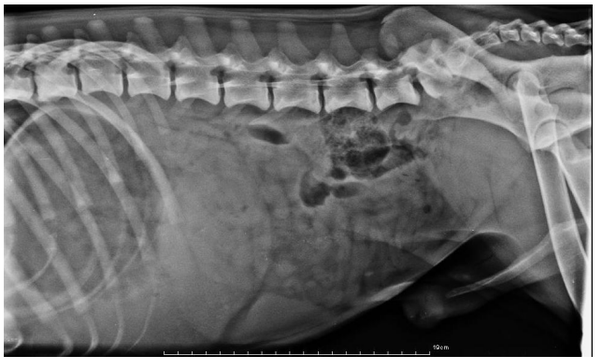

Fig. 4: Lateral view of abdomen of a dog with fibroadenoma showing increased liver opacity and a soft tissue mass in the cranial and mid abdomen pushing the stomach, intestines and spleen caudally

Ultrasonography

The size and echogenicity of liver were normal in all the six dogs of Gp I. The liver had homogenous coarse granular echogenicity with smooth margins. Both the hepatic and the portal veins were visible as anechoic areas in the liver parenchyma. Portal veins were clearly demarcated by their echogenic walls. Hepatic arteries and intrahepatic bile ducts were not differentiable in B-mode scan. The gall bladder was found as an oval to pear shaped anechoic structure with very thin wall slightly to the right of midline. The findings were similar to those described by Gupta (2010) and Nyland *et al.* (2015).

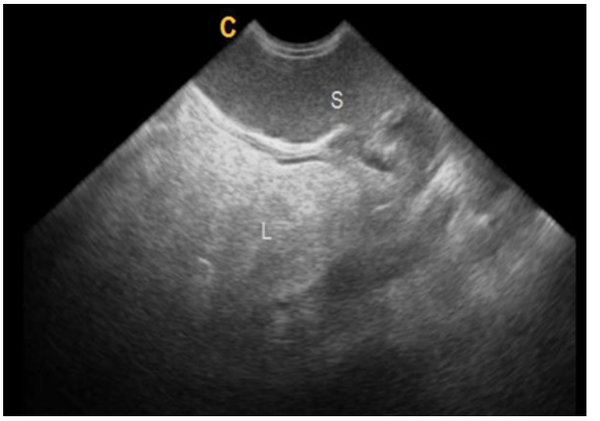

Fig. 5: Sonograms of liver with fibroadenoma showing enlargement, roundening and increased echogenicity of left hepatic lobe

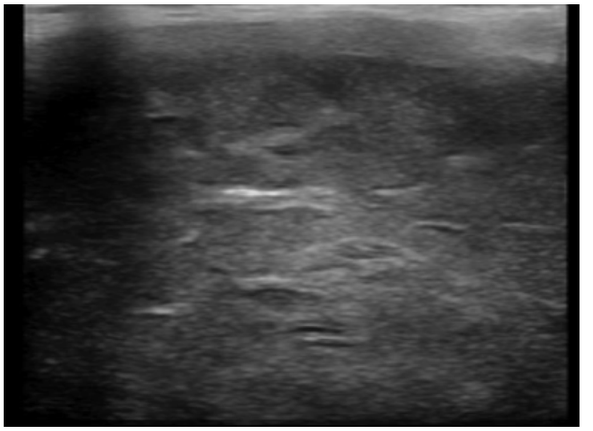

Fig. 6: Sonograms of liver with papillary adenocarcinoma showing heterogenous echogenicity of hepatic parenchyma

Ultrasonography detected hepatic abnormality in all the seven (100%) dogs of Gp II. Major ultrasonographic findings of Gp II were loss of normal echotexture, increased echogenicity of liver (n=3), roundening of hepatic margins (n=2) (Fig. 5), mixed echogenicity (n=2) (Fig. 6), hepatomegaly (n=5), presence of nodules (n=2), microhepatica (n=1) (Fig. 7) and presence of anechoic cavities separating liver lobes and other organs indicating ascites (n=3) (Fig. 8).

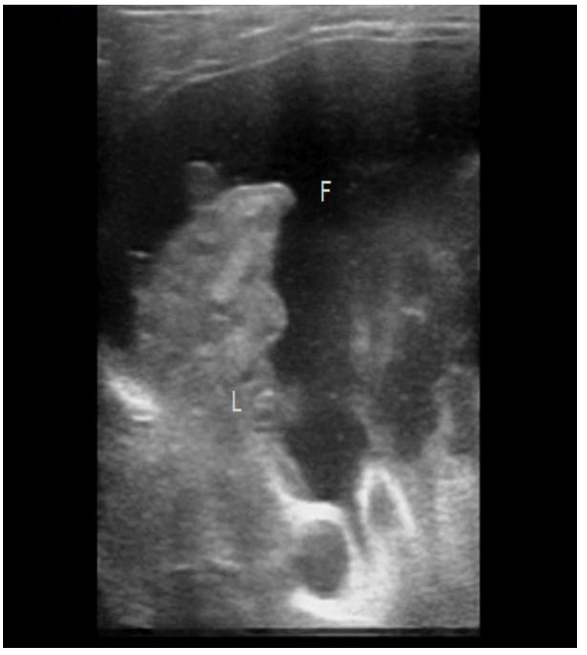

Fig. 7: Sonogram of liver with cirrhosis showing microhepatica, increased hepatic echogenicity, presence of nodules, irregular hepatic margins, and anechoic areas indicating ascites

However, the USG findings were not specific for any disease except for hepatic cirrhosis. All these findings were in concurrence with the previous reports (Nyland and Park, 1998; Shih *et al.*, 2007). In case of hepatic cirrhosis (chronic fatty liver) microhepatica, increased hepatic echogenicity, presence of hyperechoic nodules, irregular hepatic margins and anechoic areas separating hepatic lobes and other abdominal organs indicating ascites were seen on abdominal USG. Similar USG findings were reported by the earlier workers (Kumar *et al.*, 2012; Saravanan *et al.*, 2014; Elhiblu *et al.*, 2015; and Sumathi *et al.*, 2017) in cases of hepatic cirrhosis in dogs. In present study hepatomegaly, increased echogenicity, heterogenous hepatic parenchyma and presence of ascitic fluid were indicative of hepatic neoplasia.

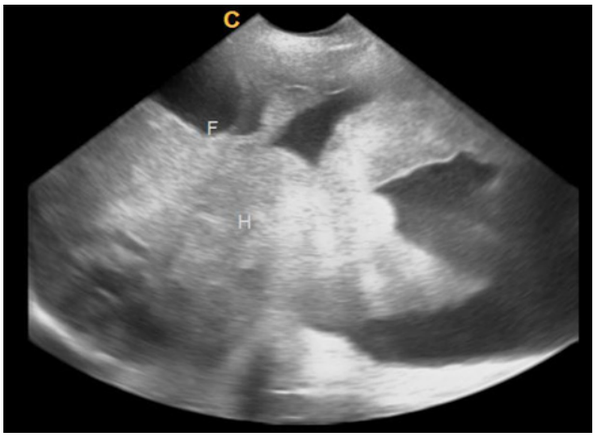

Fig. 8: Sonogram of liver with chollangiocellular carcinoma showing marked enlargement of hepatic lobe, heterogenous echotexture, roundening of hepatic margins, presence of nodular areas, irregular margins and presence of anechoic areas separating liver lobes

Similar USG findings were reported by earlier workers (Kumar *et al.*, 2012; Sumathi *et al.*, 2017) in hepatic neoplasia. However, Smith *et al.* (2012) reported marked variability in ultrasonographic appearance of lesions and no statistically significant associations between ultrasonographic appearance and diagnosis was observed. Present study also suggests that ultrasonographic findings are non specific for any disease and tentative diagnoses should not be given based on ultrasonographic findings alone and histological examination should always be considered for the confirmatory diagnosis of hepatic lesions.

Needle biopsy and histopathology

In two dogs excisional biopsy was obtained intraoperatively, whereas in remaining five dogs, ultrasound-guided biopsy was taken preoperatively. Accuracy of ultrasound guided biopsy was 100% for obtaining diagnostic sample. Different diseases diagnosed in histopathology were cholangiocellular carcinoma (n=2), chronic fatty liver/ liver cirrhosis (n=1), papillary adenocarcinoma (n=1), cystic adenocarcinoma (n=1), metastatic hemangiosarcoma (n=1), and fibroadenoma (n=1). The most common type of massive liver tumors in dogs are hepatocellular

carcinoma (HCC) and hepatocellular adenoma (Guliford and Strombeck, 1996 and Liptak, 2007). Cullen and Popp (2002) reported that HCC is the most common primary liver tumor accounting for 50% of cases, whereas bile duct carcinoma is the second most common in dogs. Chronic hepatitis is recognized and well documented liver disorder in canines (Kanemoto *et al.*, 2011). Cirrhosis is the end stage of chronic hepatitis and is irreversible and is defined as a diffuse distribution characterized by fibrosis of the liver and conversion of normal liver architecture into structurally abnormal nodules, micro and macro nodules (Elhiblu *et al.*, 2015).

CONCLUSION

The study suggests that ultrasonography is more sensitive than radiography in detection of hepatic lesions; however the USG findings are not specific for any disease except for liver cirrhosis. Laboratory tests are not specific any liver disease, however, they can be used to access the severity of the disease. It was concluded that all the diagnostic modalities evaluated viz. laboratory tests, radiography and ultrasonography complimented each other in making a diagnosis and predicting prognosis but the final diagnosis was obtained with histopathology only.

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