International Journal of Bio-resource and Stress Management https://ojs.pphouse.org/index.php/IJBSM

Crossref

IJBSM May 2024, 15(5): 01-08 **Article** AR5265a

Research Article *Natural Resource Management*

DOI: HTTPS://DOI.ORG/10.23910/1.2024.5265a

An Investigation of Canine Hepatic Dysfunction Using Different Diagnostic Methods

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0009-0001-3488-4073

ABSTRACT

The present investigation was executed at Department of Veterinary Medicine and Dr. I. P. Singh Veterinary Clinical Complex and Trauma Centre, College of Veterinary and Animal Sciences, G.B.P.U.A. & T, Pantnagar U.S. Nagar, Uttarakhand, India during the period of September, 2021 to April, 2022. The present study aimed to diagnose hepatic dysfunction in dogs presented to Dr. I.P. Singh Veterinary Clinical Complex and Trauma Centre, Pantnagar. Eighteen dogs presented with varied symptoms of hepatic dysfunction such as fever, anorexia, vomition, emaciation, polydipsia, polyuria, dullness, diarrhoea, icterus and nervous signs indicating hepatic affections were selected irrespective of their age breed, sex and were subjected to haematological, biochemical, radiographic and ultrasonographic examination. Alterations in hematobiochemical parameters of dogs with hepatic dysfunction were compared with healthy dogs. Findings of haematological examination revealed significant decrease in Hb, PCV, TEC, platelets, lymphocytes whereas there was significant increase in neutrophils in dogs with hepatic dysfunction as compared to healthy dogs. Findings of biochemical parameter revealed significant increase in total bilirubin ALT, AST, GGT, ALP whereas there was significant decrease in total protein, albumin, A:G ratio, blood glucose of dogs with hepatic dysfunction as compared to healthy dogs. Radiography and ultrasonography were found useful in diagnosis of canine hepatic dysfunction. Ultrasonography offers additional advantages over radiography by allowing for the evaluation of echogenicity, echotexture, size, shape, and margins of the liver. From the study it was concluded that combination of diagnostic test is reliable to diagnose hepatic dysfunction in dogs and single diagnostic test can be misleading.

KEYWORDS: Hepatic dysfunction, biochemical profile, bilirubin, albumin, icterus

***Citation* (VANCOUVER):** Verma et al., An Investigation of Canine Hepatic Dysfunction Using Different Diagnostic Methods. *International Journal of Bio-resource and Stress Management,* 2024; 15(5), 01-08. HTTPS://DOI.ORG/10.23910/1.2024.5265a.

Data Availability Statement: Legal restrictions are imposed on the public sharing of raw data. However, authors have full right to transfer or share the data in raw form upon request subject to either meeting the conditions of the original consents and the original research study. Further, access of data needs to meet whether the user complies with the ethical and legal obligations as data controllers to allow for secondary use of the data outside of the original study.

Conflict of interests: The authors have declared that no conflict of interest exists.

RECEIVED on 28th February 2024 RECEIVED in revised form on 25th April 2024 ACCEPTED in final form on 08th May 2024 PUBLISHED on 17th May 2024

1. INTRODUCTION

Liver, being the quintessential site for multiple physiological processes is involved in metabolic processing of nutrients, secretion and detoxification of various dangerous substances (Trefts et al., 2017; Delgado-Coello, 2021). The liver is also engaged in several critical activities, such as sustaining homeostasis, production and elimination of plasma proteins, regulation of carbohydrate and fat metabolism as well as digestion with the production of bile (Liu et al., 2017; Ozougwu, 2017). Liver is engaged in different metabolic tasks throughout the body, any factor that altering its normal physiology often causes hepatic damage. Hepatic ailments are often seen in older animals with acquired diseases and in younger animals with both acquired and congenital disease (Pallavi et al., 2017) Hepatic insufficiency refers to the liver's failure to perform its metabolic, excretory and detoxifying functions due to a drop in the number of functional hepatocytes or a change in their normal activity (Yuki et al., 2017). Hepatic dysfunction produces different clinical signs among dogs such as inappetence, vomition, diarrhoea, neurological proble, high body temperature, alteration in clotting mechanism, icterus, ascites, increasing urination and water intake (Verma et al., 2023; Sumathi et al., 2017). Dogs with hepatic dysfunction usually are asymptomatic until there is severe hepatic dysfunction and signs exhibited are often non-particular (Varshney and Hoque, 2002; Bexfield and Watson, 2009). Furthermore, it is only possible to detect functional impairment once more than 55% of the hepatic dysfunction has been reached (Elhiblu et al., 2015). The liver exhibits physiological and anatomic diversity, making it impossible to identify hepatic illness or its underlying cause with a single test. (Kumar et al., 2012). Hence, diagnosis of liver dysfunction needs haematological profile, biochemical profile, radiography and ultrasonography for effective diagnosis. Haematological profile involves evaluation of alteration in haemoglobin, packed cell volume, total erythrocyte count, total leukocyte count, platelets and differential leukocyte count. Biochemical profile involves the evaluation of increased activity of enzymes such as Alanine amino transferase, Alkaline phosphatase, Aspartate amino transferase and Gamma Glutamyl transpeptidase (Kozat and Sepehrizadeh, 2017). The increased activity of these enzymes reflects degree of tissue damage, the enzyme's intracellular concentration, and the rate of blood clearance (Oikonomidis and Milne, 2023). Inflamed or damaged liver cells release more liver enzymes into the circulation, resulting in elevated liver enzymes on blood tests. (Negasee, 2021). Other parameter includes evaluation of complete blood count, bilirubin, total protein, cholesterol, blood glucose, blood urea nitrogen and serum creatinine which are often directly or indirectly altered due to hepatic dysfunction. (Elhiblu et al., 2015). Radiography is a useful tool in diagnosing liver disease which involves detection of abnormalities in radiodensity, geometry and function (Suter, 1982) but in the presence of ascitic fluid, radiography has limitations, and the liver may appear normal in a severe diseased condition (Biller et al., 1992). Ultrasonography and liver biopsy are extremely useful in the recognition and characterization of various liver disorders such as parenchymal pathology, vascular abnormalities and biliary diseases (Nyland and Park, 1983; Kemp et al., 2013). Advanced diagnostic techniques include mass spectrometry, nuclear magnetic resonance spectroscopy and serum biomarkers (Imbery et al., 2022). Serum biomarkers such as interleukin 6, is being used as a diagnostic tool in assessing liver dysfunction (Kilpatrick et al., 2014, Schuttler and Neumann, 2015). Another biomarker includes C-reactive protein (CRP), an acute phase protein synthesized by hepatocytes has been found significantly higher in patients with cirrhosis compared to patients with hepatitis without cirrhosis in dogs (Raghu et al., 2018). This study was done to evaluate hepatic dysfunction in dogs with hematobiochemical examination, radiography and ultrasonography.

2. MATERIALS AND METHODS

The present investigation was executed at Department of Veterinary Medicine and Dr. I. P. Singh Veterinary Clinical Complex and Trauma Centre, College of Veterinary and Animal Sciences, G.B.P.U.A. & T, Pantnagar U.S. Nagar, Uttarakhand, India during the period of September, 2021 to April, 2022. Eighteen dogs presented with varied symptoms of hepatic dysfunction such as fever, anorexia, vomition, emaciation, polydipsia, polyuria, dullness, diarrhoea, icterus and nervous signs indicating hepatic affections were selected irrespective of their age breed and sex and were subjected to haematological, hematobiochemical, radiographic and ultrasonographic examination. The alteration in blood and serum parameter of these dogs with hepatic dysfunction was compared with 6 healthy dogs.

2.1. Haematological parameters

About 2 ml of blood was taken from a cephalic or saphenous vein using sterile disposable syringes in vacutainer containing EDTA with antiseptic techniques while taking all procedures Sample thus collected was marked and blood parameters of freshly collected samples were analysed for evaluation of various blood parameters as per standard laboratory procedures reported by Jain (1986)

2.2. Biochemical parameters

About 3 ml of blood was drawn in a sterile disposable syringe blood and was then transferred in vacutainer with no anticoagulant. The vacutainer was then kept at a slant

posture for about 1 hour to allow the coagulation of blood and was centrifugated for 10 minutes at 2,000 to 3,000 rpm to obtain the serum. The separated serum was then transferred in a dry Eppendorf tube using micropipette for estimation of various serum parameters using Erba diagnostics kit on a spectrophotometer. The values of different serum parameters were measured by manual calculations. Activated clotting time was calculated using a fresh blood sample by capillary method as per the method given by Hottendorf et al. (1965)

2.3. Radiography and ultrasonography

Radiographic assessment was conducted utilizing the Allengers HF X-ray apparatus, employing both lateral and ventrodorsal positioning to assess potential abnormalities in the liver. Ultrasonography was done using 5D-6000-CD VET machine using millihertz transducer (3.5 MHz) for imaging liver and other visceral organs.

2.4. Statistical analysis

The research data collected in this study was subjected to statistical analysis using unpaired t test with the help of SPSS software version 21. Tukey post-hoc analysis was used to separate the significant mean differences, with the significance threshold set at $p \leq 0.05$ (Snedecor and Cochran, 1994).

3. RESULTS AND DISCUSSION

3.1. Haematological examination

Findings of haematological examination manifested a significant decrease in mean value of haemoglobin in dogs having liver disorder in comparison to healthy dogs. This decrease in haemoglobin could be due to decreased iron absorption from intestine and reduced release from macrophages and hepatocytes because of release of hepcidin in response to IL-6 in canine portosystemic shunt and in dogs with chronic hepatic dysfunction (Grimes et al., 2012). Findings of decreased haemoglobin levels in dogs with hepatic dysfunction was also reported by Chaturvedi et al. (2013). The mean value of TEC was significantly declined in dogs affected with hepatic dysfunction. The decrease in mean value of TEC in in this study might be due to the haemolysis of RBC's due to increasing bile acids. Moreover, impaired clearance of bacteria by liver also contribute to enhanced haemolysis (Ettinger and Feldman, 2005). There was significant reduction in mean value of PCV in dogs affected with hepatic dysfunction. This drop in PCV might be attributed to a drop in disseminating red blood cells. Findings of decreased TEC and PCV was also reported by Sanjeeta et al. (2013) in dogs with hepatopathies. Neutrophil levels exhibited a significant rise in dogs afflicted with hepatic dysfunction. Neutrophilia observed in dogs with hepatic dysfunction could be due the increased cortisol production in response to increased ACTH production, increased bacterial translocation due to increased intestinal permeability. This may also occur due to loss of kuffer cells as a result of which neutrophils lasts for a longer time in circulation (Breheny et al., 2020). Increased level of neutrophil in dogs with liver impairment was also reported by Elhiblu et al. (2015). The mean value of lymphocytes reduced significantly in dogs afflicted with hepatic dysfunction. Decrease in lymphocyte in dogs with liver disorder might be in response to increase in endogenous cortisol (Harvey, 2012) and could also occur in response to viral infection such as in infectious canine hepatitis (Mosallanejad et al., 2010). Findings of reduced lymphocyte in dogs with hepatic dysfunction was also reported by Sanjeeta et al. (2013). The mean value of platelets declined significantly in dogs afflicted with liver dysfunction. This decrease in platelet count in dogs with hepatic dysfunction might be due to increased sequestration of platelets in the spleen, impaired formation of thrombopoietin by liver cells, and escalated disintegration of platelet because of aggregation in liver (Marie et al., 2021). Findings of decrease in number of platelets was also reported by Sharma et al., 2022. Other blood parameter like total leucocyte count, eosinophil, lymphocytes differ non-significantly in dogs with hepatic dysfunction (Table 1).

3.2. Biochemical examination

Findings of biochemical examination manifested a significant increase in mean value of total bilirubin in dogs with hepatic dysfunction. Increased bilirubin in dogs with hepatic dysfunction mainly occurs due to decreased bilirubin assimilation, conjugation and elimination which might be a result of intra hepatic cholestasis and reduced hepatocyte function. However increased bilirubin could not be termed as a keen indicator of hepatic disease as increased level are also associated with anaemia, increased haemolysis, cholelithiasis, pancreatitis (Lawrence and Steiner, 2017). Finding of increased total bilirubin in dogs with hepatic dysfunction was also reported by Sharma et al., 2022. The mean value of ALT in dogs afflicted with hepatic dysfunction increased significantly as compared to healthy dogs. Increased ALT activity usually arises as a result of injury to the liver cells which mainly occurs due to inflammatory disorders, ischemia, poisons, medications, or carcinogenesis (Lawrence and Steiner, 2017). Finding of increased ALT in dogs with hepatic dysfunction was also reported by Bandivadekar et al. (2020). The mean value of AST of increased significantly in dogs with liver disorder. Increased AST in hepatic dysfunction is mainly associated with degeneration and necrosis of hepatocytes (Dial, 1995). Finding of increased AST in dogs with hepatic dysfunction was also reported by Saravanan et al. (2014). The mean value of ALP increased significantly in dogs afflicted with

Table 1: Haematological and biochemical parameters in healthy dogs and dogs with hepatic dysfunction

Parameter	Healthy control (n=6)	Dogs with hepatic dysfunction (n=18)
Haemoglobin (g dl^{-1})	12.72±0.30*	9.03±0.68*
PCV (%)	47.50±1.87*	26.72±3.56*
TEC (10^6 μl^{-1})	6.40±0.15*	4.08±0.52*
TLC (10^3 μl^{-1})	10.15±0.22	19.96±2.12
Neutrophil (%)	66.50±1.95*	82.5±4.18*
Lymphocyte (%)	25.83±2.56*	13.00±3.69*
Eosinophil (%)	3.33±0.84	2.88±0.47
Monocyte (%)	3.50±0.89	1.67±0.23
Platelets (10^6 μl^{-1})	3.32±0.80*	0.94±1.28*
Total bilirubin (mg dl^{-1})	0.25±0.02*	1.82± 0.56*
ALT (IU l^{-1})	67.33±2.99*	162.11± 17.32*
AST (IU l^{-1})	43.83±3.06*	112.78± 14.23*
ALP (IU l^{-1})	62.67±3.05*	217.00±26.42*
GGT (IU l^{-1})	4.52±0.29*	19.73±5.83*
Total protein (g dl^{-1})	6.68±0.08*	5.38±0.58*
Albumin (g dl^{-1})	3.60±0.07*	2.15±0.21*
Globulin (g dl^{-1})	3.08±0.07	3.22±0.28
A: G	1.17±0.04*	0.71± 0.09*
Bun (mg dl^{-1})	18.00±0.73	16.00±3.87
Cholesterol (mg dl^{-1})	159.33±2.54	231.89±19.53
Creatinine (mg dl^{-1})	1.20±0.12	1.12±0.37
Blood glucose (g dl^{-1})	93.33±1.56*	63.12±5.82*
Clotting time (seconds)	98.63±4.26*	138.3±7.14*

Parameter bearing * in superscript differ significantly ($p \leq 0.05$)

hepatic disorder. Serum ALP activity could be raised in acute and chronic liver disorders, but more pronounced activity may indicate cholestasis. However, the highest ALP activity was seen in animals affected by cholangitis, biliary cirrhosis, or extrahepatic bile duct obstruction (Tennant and Center, 2008). Finding of increased ALP was also reported by Saravanan et al. (2014). The mean value of GGT in dogs with liver disorder escalated significantly as compared to healthy dogs. Increased serum levels of GGT are attributed to disorders of bile duct such as cholestasis or biliary hyperplasia (Lawrence and Steiner, 2017). Increased ALP activity together with raised GGT activity increases the specificity for hepatic dysfunction to 90% (Alvarez and Whittemore, 2009). Finding of increased ALP was also reported by Patel et al. (2022). Mean values of total protein and albumin in dogs with liver disorder reduced significantly as compared to healthy dogs. Hypoproteinaemia usually arises due to interference in protein metabolism as a result of hepatic dysfunction (Brovida and Rothuizen, 2010). Liver has large reserves of albumin so hypoalbunemia generally occurs in chronic liver dysfunction as is associated with condition like cirrhosis, congenital portosystemic shunt (Rothuizen, 2009). The findings of reduced total protein and albumin in dogs with hepatic dysfunction was also reported by Saravanan et al. (2014). Consequently, there was a significant reduction in mean A:G in dogs affected with hepatic dysfunction. This decrease in mean value to A: G might be attributed to the impairment in protein synthesis by the liver (Shawn, 2009). The mean value of blood glucose in dogs with liver disorder reduced significantly. This decrease in glucose in liver disorder could be due to decreased glucose synthesis and diminished insulin catabolism as a result of acute and chronic liver disorder (Schoeman, 2012). Finding of decreased blood glucose level in dogs with hepatic dysfunction was also observed by Poldervaart et al. (2009). There was a non-significant reduction in mean value of blood cholesterol in dogs with liver disorder. Hypercholesterolemia might occur due to reduced excretion of surplus cholesterol via plasma, biliary as a result of damage to hepatic parenchyma in dogs with chronic hepatitis (Assawarachan et al., 2021). Increased cholesterol in dogs with hepatic dysfunction was analogous to the findings of Secchi et al. (2012), who documented hypercholesteremia in dogs with cholestasis and biliary sludge. However other biochemical parameters like BUN, creatinine, globulin vary non-significantly in dogs with hepatic dysfunction. Finding of activated clotting time revealed a significant rise in clotting time in dogs with hepatic dysfunction. Hepatic dysfunction is accompanied by thrombocytopenia, diminished synthesis of clotting factors II, V, VII, IX, X, XI, vitamin K deficiency, abnormality in synthesis of fibrinogen, increased fibrinolysis as well as reduced levels of protein C, protein S, and antithrombin which thereby leads to increased clotting time in dogs (Lisman et al., 2010). Finding of increased clotting time was consistent with findings by Gupta et al. (2020), who opined that aberrant coagulation was attributed to decreased production of clotting factors instead of consumption.

3.3. Radiography

Radiographic examination of abdomen in lateral and ventro-dorsal view did not reveal much abnormality in many of cases but significant findings were reported in some cases which included ground glass appearance, enlarged liver. Ground grass appearance was observed in 3 (16.67%) cases. These cases revealed loss of abdominal detail of liver and other organs as a result of effusion of fluid. Findings of

ground glass appearance was also reported by Saravanan et al. (2014) in cases of ascites due to hepatic dysfunction. Enlarged liver or hepatomegaly was seen in 3 (16.67%) cases. Findings of these cases revealed increased size of liver, rounding of costo-caudal margin with the displacement of stomach caudally and displacement of diaphragm cranially. Finding also included protrusion of caudal ventral margin of liver further than the costal arch (Figure 1). Hepatomegaly in liver disorder might be attributed to hepatic congestion, hepatic abscess steroid hepatopathy, infiltration and inflammatory disease, cholestasis, cirrhosis, primary and metastatic neoplasia (Pechman, 1993; Suter, 1982). Findings of hepatomegaly in liver disorder was in accordance with Gupta et al. (2020), who reported hepatomegaly characterized by extension of hepatic lobes beyond rib cage in 2 dogs out of 7 dogs suffering from various liver disorder (Figure 2).

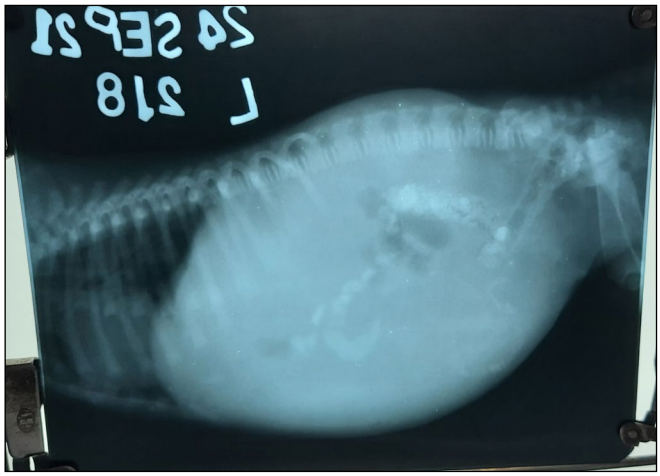

Figure 1: Radiograph of a dog affected with hepatic dysfunction indicating ascites

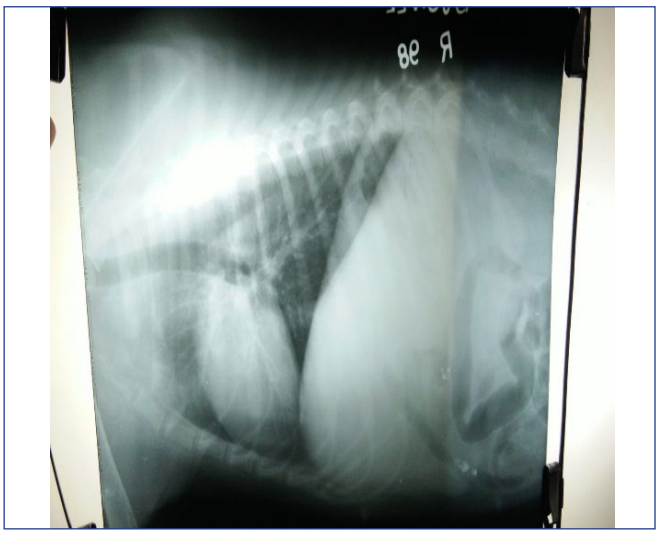

Figure 2: Radiograph of a dog affected with hepatic dysfunction indicating hepatomegaly

3.4. Ultrasonography

Ultrasonography was performed as a diagnostic test in dogs with liver dysfunction and revealed mild hyperechoic liver along with floating of abdominal organs in affected with ascites. Findings of hyperechoic liver in dogs affected with ascites was also reported by Lakshmi and Padmaja, (2022). Findings in 5 (27.78%) cases included hyperechoic liver with smooth margins which could be due to chronic hepatitis. Hyperechoic texture could be due to increased blood circulation, cellular infiltration and fibrosis of liver in chronic hepatitis **(**Webster, 2005) (Figure 3). Findings also included hypoechoic texture of liver parenchyma with extended visualization of portal vessels in 7 (38.89%) which could be due to acute hepatitis. Findings of hypeochoic liver were also reported by Patel et al. (2022) in cases of dogs with acute hepatic dysfunction (Figure 4). Other findings

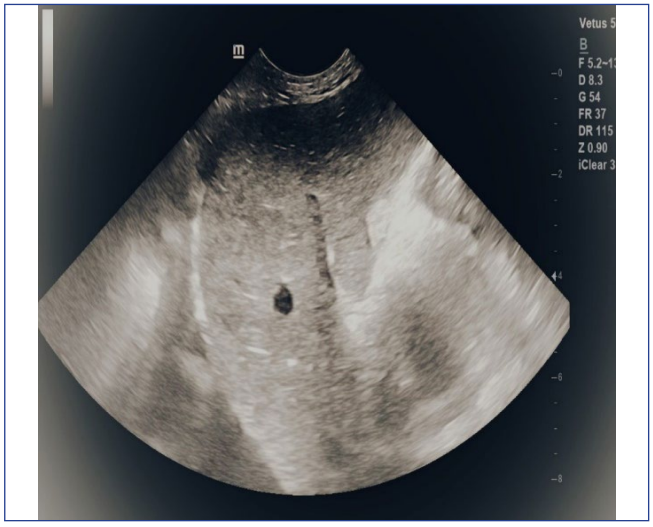

Figure 3: Ultrasonograph indicating hyperechoic liver with smooth margins in a dog affected with hepatic dysfunction

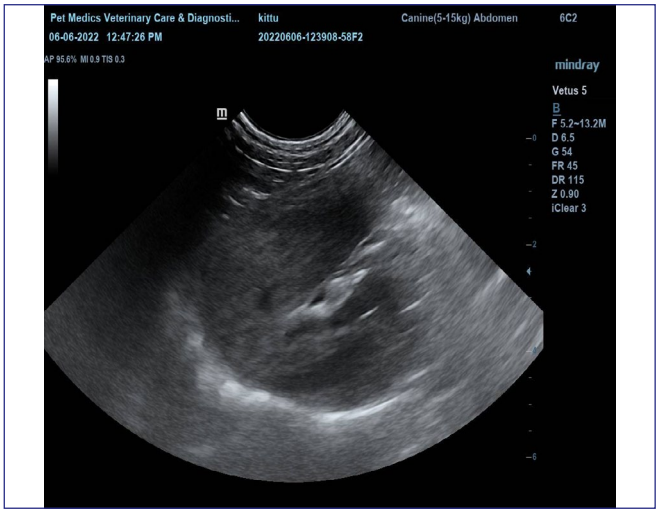

Figure 4: Ultrasonograph indicating hypocheoic liver with distinct portal vessels in a dog affected with hepatic dysfunction

included enlarged liver and rounding of hepatic margins with increase in echogenicity indicating hepatomegaly in 3 (16.67%) dogs. These findings were in agreement with Lakshmi and Padmaja (2022), who reported hepatomegaly characterized by increased size of liver between stomach and diaphragm with rounded caudal margins which is particularly noticeable in steroid hepatopathy, fatty liver, congestive hepatopathy, acute hepatitis, inflammation, and hepatic tumor (Figure 5).

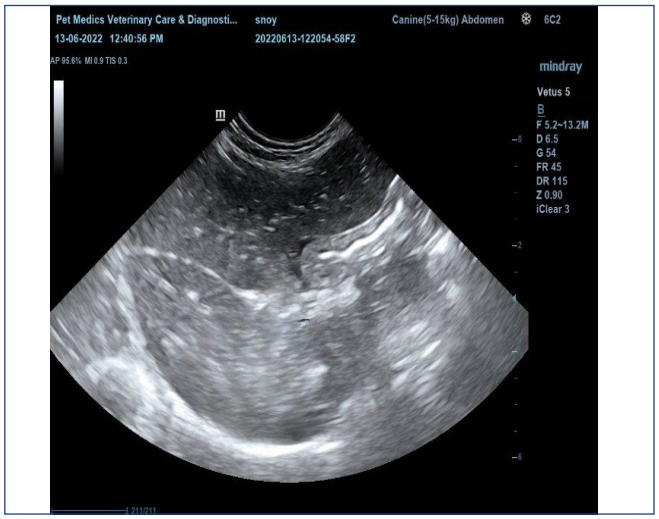

Figure 5: Ultrasonograph indicating hepatomegaly with round liver margins in a dog affected with hepatic dysfunction

4. CONCLUSION

The study highlighted the importance of a combination of diagnostic procedures for a reliable diagnosis of hepatic dysfunction in dogs. Radiography and ultrasonography were two important procedures in diagnosing hepatic dysfunction in dogs. Ultrasonography had additional advantages over radiography by allowing for the evaluation of echogenicity, echotexture, size, shape, and margins of the liver. Integration of hematobiochemical examinations with radiographic and ultrasonographic findings was helpful in better understanding hepatic dysfunction, which contributed to better diagnosis and effective treatment planning.

5. ACKNOWLEDGEMENT

The authors are thankful to Dean college of veterinary and Animal science, Pantnagar for providing necessary facilities during the study.

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