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The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2022; SP-11(9): 2468-2471

www.thepharmajournal.com
Received: 20-06-2022
Accepted: 27-07-2022

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Serum biochemical profile of dogs with hepatic disorders

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Abstract
The study was undertaken in 9925 clinical cases presented to the Teaching Veterinary Clinical Complex, WBUAFS, Belgachia, Kolkata. The diagnosis was done using preliminary examination along with radiography and ultrasonography for confirmatory diagnosis. A group of 10 healthy control dogs were studied for the trial. 72 (0.73%) dogs were diagnosed with hepatic disorders. Dogs with clinical signs showing inappetance, vomiting, yellowish tinge in skin and mucus membrane, depriciating body condition, diarrhoea, anorexia, weight loss, pale mucus membrane, hepatomegaly, abdominal pain, ascites, constipation, pyrexia, darker color of urine, polydipsia and polyuria were considered for the study. Dogs with hepatic disorders showed increase in BUN (Blood Urea Nitrogen), creatinine, AST (Aspartate Amino Transferase), ALT (Alanine Amino transferase), CRP (C reactive Protein), ALP (Alkaline Phosphatase), GGT (Gamma Globulin Transferase), SBA (Serum Bile Acid), direct bilirubin, indirect bilirubin and total bilirubin.

Keywords: Dogs, Anaemia, hepatic disorder, liver, serum biochemistry

Introduction
The growing pet-dog industry is considered a boon for humans looking for the most pure form of affection in the form of their furry companions. However, for the animal, it is a boon as well as a bane. Living with humans has altered the lifestyle of these dogs, their food and habits. So many fall prey to the use of over and under dosage of medicines, over the counter medication, feed not meant for species other than humans and lack of activity due to living in confined spaces. The organ in the body that seems to be affected the most is the liver. 5% of the non communicable diseases that occur in dogs are liver diseases. 70% of these diseases again are chronic diffuse liver diseases (Watson, 2017; Smirnova *et al.*, 2018; Belza *et al.* 2017; Vatnikov *et al.*, 2019; Popova, *et al.* 2020) [52, 42, 4, 50, 31]. The liver being a highly compensatory machine of the body; clinical, laboratory and instrumental methods fail to bring to light, the focal points of liver disorder diagnosis (Tikhonchuk *et al.*, 1992; Vatnikov *et al.*, 2015; Popova *et al.*, 2020) [45, 50, 31]. This study is an attempt at evaluating the serum biochemical parameters that indicate deficiencies in the functioning of the liver.

2. Materials and Methods
The present investigation was carried out in the Department of Veterinary Medicine, Ethics and Jurisprudence, Faculty of Veterinary and Animal Science, West Bengal University of Animal and Fishery Sciences, Kolkata from 15th September, 2019 to 15th March, 2022. Ten apparently healthy dogs presented to the Veterinary Clinical Complex (Belgachia) were considered as controls. These animals had been presented with complaints of lethargy, weakness, yellowish skin, mucus membrane and eyeball coloration, pale or whitish mucus membrane and gums, Vomition, diarrhea, constipation, inappetance leading to anorexia, melena, distended abdomen, yellowish urine coloration, polydipsia, polyuria, dehydration represented by sunken eyeballs and congested mucus membranes and gradual weight loss. Dogs with these symptoms were however exempted from the study if they were tested positive for any kind of bacterial, viral or Protozoal infection or parasitic infestation of the gut. All suspected cases were subjected to radiography and ultrasonography for confirmatory diagnosis.

2.1 Serum biochemical examination

Five millilitres of whole blood was collected into a plain vacutainer and was kept still for 20 minutes. The serum was separated from the coagulated blood by centrifuging the clotted blood at 3000 rpm for 15 minutes and the separated serum was transferred to sterile Eppendorf tube (1.5 ml) with the help of Pasteur pipette and the following estimations were doing using VetTest 8008 auto analyzer from Idexx and Bensphera spectrophotometer. Total Serum Protein (g/dL), Serum Albumin (g/dL), Serum Globulin (g/dL), Blood Urea Nitrogen (BUN) (mg/dL), Creatinine (mg/dL), Bilirubin (mg/dL), Glucose (mg/dL), Indirect bilirubin (mg/dL), Direct bilirubin (mg/dL), Total bilirubin (mg/dL), Alanine Aminotransferase (ALT) (IU/L), C reactive protein (CRP) (mg/L), Alkaline Phosphatase (ALP) (IU/L), Gamma Glutamyl Transferase (GGT) (IU/L), Serum Bile acids (SBA) (µmol/L) and AST (IU/L) were evaluated using commercially available kits by ERBA Diagnostic Mannheim GmbH.

2.2 Statistical analysis

Data were analyzed by one-way analysis of variance (ANOVA), with post hoc analysis using Duncan's multiple comparison tests using SPSS 20.0 software and expressed as mean±SE with $p<0.05$ considered statistically significant (Snedecor and Cochran, 1994) [43].

3. Results and Discussion

Table 1: Comparison of mean (+/- standard error) of serum biochemical parameters between healthy control and diseased dogs

Parameter	Healthy dog (n = 10)	Diseased dog (n = 72)
Protein (g/dL)	6.30 ± 0.57	5.52* ± 0.06
Albumin (g/dL)	3.35 ± 0.50	2.69* ± 0.08
Globulin (g/dL)	2.95 ± 0.07	2.82 ± 0.105
BUN (mg/dL)	19.78 ± 1.23	27.94* ± 0.62
Creatinine (mg/dL)	0.76 ± 0.03	1.44* ± 0.03
AST (IU/L)	33.89 ± 2.11	181.44* ± 14.41
Glucose (mg/dL)	88.5 ± 1.12	76.69* ± 3.23
ALT (IU/L)	52.89 ± 3.34	187.83* ± 10.45
CRP (mg/L)	8.54 ± 0.18	32.17* ± 1.15
ALP (IU/L)	59.72 ± 3.95	225.61* ± 8.15
GGT (IU/L)	7.97 ± 0.19	31.00* ± 3.53
SBA (µmol/L)	2.24 ± 6.32	42.26 * ± 4.56
Bilirubin (mg/dL)	0.34 ± 0.004	1.49* ± 0.14
Direct bilirubin (mg/dL)	0.22 ± 0.004	1.034* ± 0.097
Indirect bilirubin (mg/dL)	0.115 ± 0.006	0.45* ± 0.068

(* indicates values significant at $p<0.05$)

The serum biochemical parameters were assessed to confirm the diagnosis of hepatic disorder. The mean ± SE values comparing the diseased animal with the healthy control have been represented in tabular form (Table 1). While the serum levels of total protein, albumin and glucose are seen to lower significantly ($p<0.05$) in the dogs with hepatic disorders, the values of BUN, creatinine, AST, ALT, CRP, ALP, GGT, SBA, total bilirubin, direct bilirubin and indirect bilirubin are seen to be higher significantly ($p<0.05$).

Increase in the levels of indirect bilirubin in liver disorder was previously reported by Twedt (1998) [47], Neuumann (2004) [29], Rothuizen (2009) [34] and Kozat and Sepehrizadeh (2017) [22]. Increase in the levels of direct bilirubin were observed by Rothuizen (2009) [32], Kozat and Sepehrizadeh (2017) [22] and Lakshmi and Padmaja (2021) [26]. Total bilirubin levels rise has been previously reported by Lakshmi and Padmaja (2021) [26], Lakshmi *et al.* (2018) [25], Tantary *et al.* (2014) [44], Saravanan *et al.* (2014) [37] and Chohan *et al.* (2007) [11]. The disturbed balance between the rate of production, metabolism and excretion of bilirubin explains hyperbiliruminaemia in hepatic disorders (Tantary *et al*. (2014)) [44].

Rise in serum bile acid levels in dogs with hepatic disorder have been reported by Center *et al.* (1985) [8], Kim *et al.* (1986) [21], Schlesinger and Rubin (1993) [39], Neumann *et al.* (2007) [29], Ruland *et al.* (2010) [35] and Pena-Ramos *et al.* (2021) [30]. In liver diseases, the reduced functional hepatocyte mass or inefficient shunting of blood past the hepatocyte result in systemic bile acid levels to approach those present in the portal circulation (Gilmore and Hofmann, 1980) [16].

Elevated values of GGT in hepatic disorder in dogs had previously reported by Bunch *et al.* (1982) [7], Kraft *et al.* (1983) [23], Hall and German (2005) [18] and Chohan *et al.* (2007) [11]. The elevation in levels of cholestatic enzymes like GGT occurs due to endocrine disorders, cholestasis, neoplasia, benign nodular hepatic hyperplasia and intake of certain drugs besides occurring idiopathically in certain breeds (Alvarez and Whittemore, 2009) [3].

Increase in ALP have been observed before this study by Secchi *et al.* (2012) [40], Saravanan *et al.* (2014) [37], Tantary *et al*. (2014) [44], Elhiblu *et al.* (2015) [13] and Lakshmi and Padmaja (2021) [26]. It has been attributed to hepatocellular injury.

Walker (1990) [51], Toulza *et al.* (2006) [46], Gow *et al.* (2012) [17] and Covin and Steiner (2022) [12] have reported increased levels of CRP in serum of dogs with hepatic disorders earlier. Fatty infiltration of liver could trigger inflammatory processes releasing CRP. Cytokines produced in other tissues resulting in metabolic abnormalities characterizing insulin resistance are considered another source of CRP production Kerner *et al.* (2005) [20].

Alteration in values of glucose in dogs with hepatic disorders was reported earlier by Hall and German (2005) [18], Gattani and Gupta (2011) [15], Tantary *et al*. (2014) [44] and Lakshmi and Padmaja (2021) [26]. Webster (2010) [53] reported decrease in values of glucose in dogs with hepatic disorders and regarded it to be the consequence of marked reduction in liver function.

Alan (2008) [2] stated a decrease in circulating blood urea nitrogen in dogs with hepatic dysfunctions due to decreased production of urea from ammonia. Hall and German (2005) [18] reported altered values of BUN in cases of hepatic disorder. Gattani and Gupta (2011) [44], Tantary *et al*. (2014) [33] and Lakshmi and Padmaja (2021) [48] also reported increase in BUN values as documented in the present study. This increase in BUN could be explained by the impaired kidney functions associated with liver disorders due to decreased capacity of the liver to detoxify the harmful products.

Lakshmi and Padmaja (2021) [26], Prebavathy *et al*. (2020) [33], Jeena (2019) [19], Lakshmi *et al.* (2018) [26] and Elhiblu *et al.* (2015) [13] had also previously reported decrease in total protein. Brovida and Rothuizen (2010) [6] explained the decrease in total protein as a clinical consequence of disruption of hepatic protein metabolism.

Increases in the ALT levels in dogs with systemic hepatic dysfunctions have been earlier observed by Sarma *et al.* (2009) [38]. Shrivastava *et al*. (2010) [41], Bexfield *et al*. (2011) [5], Tantary *et al*. (2014) [44], Lawrence (2015) [27] and Pradeep *et al.* (2017) [32]. This increase in ALT levels can be explained by hepatocellular injury.

Hall and German (2005) [18] reported that creatinine values

were affected in cases of liver disorder. In 2015, Elhiblu *et al.* [13] reported higher levels of creatinine in dogs with hepatic distress. The increase in creatinine could be attributed to the impaired kidney function associated with liver disorders due to decreased capacity of the liver to detoxify the harmful products (Sampaio *et al.*, 2014) [36]. However, in contrast to this study, Alvarez and Whittemore (2009) [3] had reported that creatinine levels remained unaffected in dogs with liver disorders.

Hypoalbuminemia as a result of distress to the liver was observed in the study and Brovida and Rothuizen (2010) [6] explained it as an outcome of disruptive hepatic protein metabolism in cases of chronic hepatic disorders. Chaturvedi *et al.*, (2013) [10] had also reported German (2005) [23], Chohan *et al*. (2007) [1], Jeena (2019) [24] and Prebavathy *et al.* (2020) [33] Increase in AST in cases of hepatic disorder was explained by leakage of the enzyme due to compromised membrane integrity of the cells. Although AST is also present in kidney, brain, cardiac and skeletal muscles, 80% of it resides in hepatocyte cytosol (Center, 2007) [9].

4. Summary and Conclusion

Analysis of the serum biochemical parameters in dogs with hepatic disorders point out towards the fact that these factors are reliable diagnostic tools and help in early detection of the condition. hypoalbuminemia in ascitic dogs.

Increase in AST levels in hepatic disorders have been previously observed by Kraft *et al.* (1983) [23], Abd-el-Kader and Hauge (1986) [1], Kramer and Hoffman (1997) [24], Hall and

5. References

1. Abdelkader SV, Hauge JG. Serum enzyme determination in the study of liver disease in dogs. Acta, Veterinaria, Scandinavica. 1986;27(1):59-70.
2. Alan. A case oriented approach to liver laboratory profiling in dog and cats. WSAVA/FECAVA World Small Animal Congress. c2008. p. 551-553.
3. Alvarez L, Whittemore JC. Liver enzyme elevations in dogs: physiology and pathophysiology. *Compend contin* Educ Vet. 2009;31(9):408-10, 412-3; quiz 414. PMID: 20180206.
4. Belza C, Thompson R, Somers GR, deSilva N, Fitzgerald K, Steinberg K, *et al*. Persistence of hepatic fibrosis in paediatric intestinal failure patients treated with intravenous fish oil lipid emulsion. Journal of Paediatric Suregry. 2017;52:795-801.
5. Bexfield NH, Andres-Abdo C, Scase TJ, Constantino-Casas F, Watson PJ. Chronic hepatitis in the English springer spaniet: clinical presentation, histological description and outcome. The Veterinary Record. 2011;169(16):415.
6. Brovida S, Rothuizen J. Liver and Pancreatic diseases. In: Ettinger, S. J. and Feldman, E. C. (Eds). Textbook of Veterinary Internal Medicine. 7th Edition. (Elsevier Saunders Co., St. Louis); c2010. p. 1609-1690.
7. Bunch SE, Castlemam WS, Hornbuckle WE, Termant BC. Hepatic cirrhosis associated with long term anticonvulsant drug therapy in dogs. Journal of American Veterinary Medical Association. 1982;181:357-362.
8. Center SA, Baldwin BH, Erb HN, Tennant BC. Bile acid concentrations in the diagnosis of hepatobiliary disease in the dog. Journal of the American Veterinary Medical Association. 1985;187(9):935-940.
9. Center SA. Interpretation of Liver Enzymes. Veterinary Clinics of North America: Small Animal Practice. 2007;37(2):297-333.
10. Chaturvedi M, Gonaie AH, Shekawat MS, Chaudhary D, Jakhar A, Chaudhari M. Serum haemato-biochemical profile in ascitic dogs. Haryana Veterinarian. 2013;52:129-130.
11. Chohan AS, Bansal BK, Randhaw CS, Dhaliwal PS. Liver dysfunctions in dogs. Indian Veterinary Journal. 2007;84(10):1042-1044.
12. Covin MA, Steiner JM. Measurement and clinical applications of C-reactive protein in gastrointestinal diseases of dogs. Veterinary Clinical Pathology. 2022;50:29-36.
13. Elhiblu MA, Dua K, Mohindroo J, Mahajan SK, Sood NK, Dhaliwal PS. Clinic-haemato-biochemical profile of dogs with liver cirrhosis. Veterinary World. 2015;8(4):487-491.
14. Ettinger SJ, Feldman EC. Liver and pancreatic diseases. In: Textbook of Veterinary Internal Medicine, 6th Edn. (Elsevier Saunders Co., St. Louis); c2005. pp. 1421-1495.
15. Gattani A, Gupta SR. Ascites in dog – A case report. Indian Journal of Field Veterinarians (The). 2011;7(2):72-73.
16. Gilmore IT, Hofmann AF. Altered drug metabolism and elevated serum bile acids in liver disease: a unified pharmacokinetic explanation. Gastroenterology. 1980;78(1):177-179.
17. Gow AG, Marques AI, Yool DA, Crawford K, Warman SM, Eckersall PD, *et al*. Dogs with congenital porto-systemic shunting (cPSS) and hepatic encephalopathy have higher serum concentrations of C-reactive protein than asymptomatic dogs with cPSS. Metabolic brain disease. 2012;27(2):227-229.
18. Hall EJ, German AJ. Laboratory evaluation of hepatic disease, *In.* BSAVA Manual of Canine and Feline Clinical Pathology, *Edt.* Villiers., E and Blackwood, L. Edn. 2nd, (BSAVA, Gloucester, UK.); c2005. p. 184-206.
19. Jeena A. Diagnosis and clinic-therapeutic studies on canine hepatic dysfunction. M.V.Sc. thesis (Veterinary Medicine), G.B. Pant University of Agricultural & Technology, Pantnagar; c2019.
20. Kerner A, Avizohar O, Sella R, Bartha P, Zinder O, Markiewicz W, *et al*. Association between Elevated Liver Enzymes and C-Reactive Protein. Possible Hepatic Contribution to Systemic Inflammation in the Metabolic Syndrome. Atherosclerosis, thrombosis and vascular biology. American Heart Association. 2005;25(1):193-197.
21. Kim MJ, Suh DJ. Profiles of serum bile acids in liver diseases. Korean Journal of Internal Medicine. 1986;1(1):37-42.
22. Kozat S, Sepehrizadeh E. Methods of Diagnosing in Liver Diseases for Dog and Cats. Turkish Journal of Scientific Reviews. 2017;10:26-36.
23. Kraft W, Ghermai AK, Winzinger H, Knoll L. Comparison of serum activities of aspartate amino transferase, alanine amino transferase, glutamate dehydrogenase, alkaline phosphatase and gamma glutamyl transferase in diagnosis of liver diseases in the dogs. Berliner and Munchener, Tierarztliche, Wochenschrift. 1983;96(12):421-422, 425-431.
24. Kramer JW, Hoffman WE. Clinical enzymology. In: Clinical biochemistry of domestic animals. Edt. Kaneko,

J., Harvey, J. and Bruss, M. (Academic Press London); c1997. p. 330.
25. Lakshmi K, Padmaja K, Nagaraj P, Gopala Reddy A, Gnana Prakash M. Haemato-Biochemical studies of hepatobiliary disorders in dogs. International Journal Current Microbiology Applied Sciences. 2018;7(01):1406-1411.
26. Lakshmi K, Padmaja K. Biochemical evaluation of canine hepatic disorders. The Pharma Innovation Journal. 2021;10(1):24-26.
27. Lawrence Y. Canine chronic hepatitis: diagnosis and treatment. Today's Veterinary Practice March/April; c2015. p. 26-33.
28. Neumann S, Welling H, Thuere S. Evaluation of serum L-phenylalanine concentration as indicator of liver disease in dogs: a pilot study. Journal of the American Animal Hospital Association. 2007;43(4):193-200.
29. Neumann S. Comparison of blood parameters in degenerative liver disease and liver neoplasia in dogs. Comparative Clinical Pathology, 2004;12(4):206-210.
30. Pena-Ramos J, Barker L, Saiz R, Walker DJ, Tappin S, Hare C, *et al*. Resting and postprandial serum bile acid concentrations in dogs with liver disease. Journal of Veterinary Internal Medicine. 2021;35:1333-1341.
31. Popova I, Shabunin S, Vatnikov Y, Yagnikov S, Karamyan A, Babichev N, *et al*. Integral Intoxication Indices in Liver Diseases in Dogs: Clinical Characteristics and Relevance. Liver. 2020;4:5.
32. Pradeep K, Yathiraj S, Ramesh PT, Leena G, Narayanswamy HD. Clinico-Haemato-Biochemical and Ultrasonographic alterations in dogs with non infectious hepatic disorders associated with hypo-albuminemia. International Journal of Advanced Biotechnology and Research. 2017;7(3):585-589.
33. Prebavathy T, Amaravathi P, Rajesh K, Vaikuntarao V, Bharathi S, Raghunath M. Haematobiochemical alterations in hepatic diseases in dogs. Journal of Entomology and Zoology Studies. 2020;8(5):1382-1384.
34. Rothuizen J. Important clinical syndromes associated with liver disease. Veterinary Clinics: Small Animal Practice. 2009;39(3):419-437.
35. Ruland K, Fischer A, Hartmann K. Sensitivity and specificity of fasting ammonia and serum bile acids in the diagnosis of portosystemic shunts in dogs and cats. Veterinary Clinical Pathology. 2010;39(1):57-64.
36. Sampaio MS, Martin P, Bunnapradist S. Renal dysfunction in end-stage liver disease and post-liver transplant. Clinics in liver disease. 2014;18(3):543-560
37. Saravanan M, Mondal DB, Sarma K, Mahendran K, Vijayakumar H, Sasikala V. Comprehensive study of haematobiochemical, ascetic fluid analysis and ultrasonography in the diagnosis of ascites due to hepatobiliary disorders in dog. Indian Journal of Animal Sciences. 2014;84(5):503-506.
38. Sarma K, Das G, Konwar B, Bayan H, Ali A. Haemato-biochemical Profile of canine ascites. Indian Journal of Veterinary Medicine. 2009;29(2):121-122.
39. Schlesinger DP, Rubin SI. Serum bile acids and the assessment of hepatic function in dogs and cats. The Canadian Veterinary Journal. 1993;34(4):215.
40. Secchi P, Poppl AG, Ilha A, Kunert Filho HC, Lima FES, Garcia AB, *et al*. Prevalence, risk factors and biochemical markers in dogs with ultrasound-diagnosed biliary sludge. Research in Veterinary Science. 2012;93(3):1185-1189.
41. Shrivastava S, Gupta N, Gupta DK, Shukla PC. Haematological and enzymatic alterations associated with hepatic disorders in canines. Intas Polivet, 2010, 11(2).
42. Smirnova IP, Kuznetsova OM, Shek D, Ivanova-Radkevich VI, Sachivkina NP, Gushchina YS. Investigation of the immunogenic properties of anti tumor enzyme l-lysine-alpha-oxidase. FEBS Journal. 2018;8(S1):234.
43. Snedecor GW, Cochran WG. In: Statistical Methods Viii Edn. Oxford and IBH Publishing Company, New Delhi; c1994.
44. Tantary HA, Soodan JS, Chrirag S, Ansari MM, Kumar S, Imtiyaz T. Diagnostic studies in dogs with hepatic disorders. International Journal of Veterinary Science. 2014;3(4):210-215.
45. Tikhonchuk VS, Ushakov IB, Karpov VN. Possibilities of using new integral indicators of human peripheral blood. Military Medical Journal. 1992;3:27-31.
46. Toulza O, Center SA, Brooks MB, Erb HN, Warner KL, Deal W. Evaluation of plasma protein C activity for detection of hepatobiliary disease and portosystemic shunting in dogs. Journal of the American Veterinary Medical Association. 2006;229(11):1761-1771.
47. Twedt DC. Diagnosis of liver disease in companion animals. Veterinary Quarterly. 1998;20(1):S44-S46.
48. Varshney JP, Hoque M. Clinico-pathological and ultrasonographic observations in canine hepatopathies. Indian Journal of Animal Science. 2002;72:423-427.
49. Vatnikov YA, Sakhno NV, Sotnikova ED, Kulikov EV, Parshina VI. Clinical control of packed RBC transfusion in acute surgical pathology such as gastric dilation and volvulus in dogs. Biomedical and Pharmacology Journal. 2015;8(2):711-717.
50. Vatnikov YuA, Kulikov EV, Kubatbekov TS, Kuznetsov VI, Sturov NV, Shirmanov VI. Diagnosis of violations of microcalculation in the late recovery period after thrombosis of cerebral vessels. Prensa Medica Argentina. 2019;105(1):1000335.
51. Walker FJ. Protein C deficiency in liver disease. Annals of Clinical and Laboratory Science. 1990;20(2):106-112.
52. Watson P. Canine Breed-Specific Hepatopathies. Veterinary Clinical North American Small Animal Practice. 2017;47(3):665-682.
53. Webster CRL. History, clinical signs and physical findings in hepatobiliary disease. In: Text book of Veterinary Internal Medicine, Ettinger, S.J. and Feldman, E. (Eds) 7th edition. (St. Louis, Elsevier Saunders); c2010. p. 1612-1618.