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Research Articles

Diabetes mellitus induced reactive hepatopathy in dogs

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Abstract

The present study was carried out on dogs presented with history of clinical signs as anorexia, fatigue, polydipsia, polyuria, polyphagia, exercise intolerance, jaundice, ascites, cachexia, seizures etc. The haematological parameters in affected dogs varied non significantly as compared to healthy animals except MCV and MCH which increased significantly. The mean values of ALT, AST, ALP, GGT, Glucose, BUN and Creatinine were significantly increased whereas mean values of albumin were significantly decreased compared to healthy animals indicative of altered liver and renal functioning. On the basis of detailed clinical and haemato-biochemical examination, out of a total of 54 dogs with reactive hepatopathy, 8 dogs suffered from Diabetes Mellitus leading to concurrent liver disorder. The dogs suffering from diabetic hepatopathy were in the age group of 4 – 14 years with maximum incidence in 6-8 years of age. It was concluded that apart from varied causes of reactive hepatopathy in dogs, Diabetes Mellitus was an important cause of liver disorder.

Key words: Reactive hepatopathy, Diabetes mellitus, Diabetic dogs, Hyperglycaemia, Liver enzymes

Liver is the largest parenchymal organ which is involved with almost all of the biochemical pathways that allow growth, fight diseases, supply nutrients, provide energy and aid reproduction. It is vital and complex organ of the body which is susceptible to many adverse effects of drugs, chemicals, infectious agents, autoimmune disease, along the idiopathic occurrence (Ahmedullah *et al*., 2008). Thus, maintaining a healthy liver is crucial for the overall health and well-being of life of animals (Aashish *et al*., 2012). Any factor that significantly alters the physiology will often produce hepatic damage. Such damage may result from infectious, metabolic, toxic, degenerative, congenital or neoplastic diseases which further may be because of many reasons or diverse sources.

Reactive hepatitis is an inflammatory disorder of the liver induced by an extra hepatic process. It is associated with disorders of many other organs apart from the liver including gastrointestinal and respiratory diseases, heart failure and diseases of the urinary and reproductive system (Negasee, 2021). Different inflammatory mediators cytokines such as Interleukin-1 (IL-1), Interleukin-6 (IL-6) and Tumor Necrosis Factor- (TNF-) are released as lipopolysaccharide (LPS) can activate kupffer cells in the liver parenchyma. A consequence of this activation is the release of pro-inflammatory cytokines that induces leukocyte migration and therefore induces reactive hepatitis results excessive damage of liver cells (Elhiblu *et al*., 2015).

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Endocrine diseases are imbalances in hormone levels which can affect pet's health in many ways. Diabetes mellitus, hyperadrenocorticism (Cushing's disease), and hyperthyroidism can all cause impaired liver function because of their effects on the organ (Ming et al. 2015). In view of unscientific feeding, ever increasing environmental pollution and abuse of common therapeutic agents and stress, like human beings, the animals are also becoming more susceptible to hepatic dysfunction. The perusal of records of Veterinary Clinics, DGCN COVAS reveals that clinical cases of diabetic hepatopathy in dogs are also presented. Thus, the present study on haematobiochemical alterations in diabetes induced reactive hepatopathy in dogs was undertaken for better management of this condition.

Materials and Methods

The present study was carried out on dogs presented during the period of August, 2016 to April, 2019 in the Department of Veterinary Medicine in Veterinary Clinical Complex of College of Veterinary & Animal Sciences, CSKHPKV Palampur (H.P). Preliminary screening was done on the basis of the patient's history and information provided by the owner and presenting clinical signs as anorexia, fatigue, polydipsia, polyuria, polyphagia, exercise intolerance, jaundice, ascites, cachexia and seizures. Besides this, haemato-biochemical estimation and imaging techniques (radiology and ultrasonography) were used for confirmatory and

Table 1. Classification of hepatic dysfunction cases in dogs

S. No.	Etiology	Total no. of cases	% out of total cases
I.	Hepatic Diseases / Primary Hepatitis	102	(65.38%)
II.	Extrahepatic diseases/ Reactive Hepatitis	54	(34.62%)
	Total Cases	156	
	Reactive Hepatic Diseases	54	
	Diabetes mellitus	8 (14.82%)	5.13%

differential diagnosis of hepatic dysfunction. On this basis, a total of 156 dogs suffering from hepatic dysfunction were included in the present study. A total of 12 clinically healthy adult dogs formed the control group. Dogs presented for regular vaccination, routine health check-up and elective surgery were included in this group irrespective of age, sex and breed.

Results and Discussion

Of all the cases presented during the above period, a total of 156 dogs suffering from various hepatic dysfunctions were included in the present study. Out of these cases, a total of 102 dogs were found to be suffering from Primary Hepatic diseases representing a total of 65.38% cases. Another 54 dogs suffered from Reactive Hepatic diseases representing a total of 34.62 % cases. Out of these 54 reactive hepatopathy cases, 8 dogs suffered from Diabetes Mellitus representing 14.82% of reactive cases and 5.13% of total hepatopathy cases (Table 1).

Induced reactive hepatitis in this study was also composed of endocrine disorders, mainly diabetes mellitus. The results are in accordance with Neumann and Danner (2012) who also found reactive hepatitis in patients with endocrine disorders. The possible mechanism in these cases could be the accumulation of glycogen and lipids, which may induce cell degeneration with secondary infiltration of inflammatory cells.

The most common clinical signs observed were inappetance, anorexia, polydipsia, polyuria, whereas vomiting was lesser commonly observed. These signs are similar to those observed by Neumann and Danner (2012) and Jena *et al*., (2019) who observed inappetence, polyuria/polydipsia, vomiting or diarrhea in 55 and 34 clinical cases of reactive hepatitis and diabetic dogs respectively.

The mean values of rectal temperature, respiration rate and heart rate are presented below in Table 2. The mean values of rectal temperature and respiration rate varied non significantly whereas heart rate was significantly higher than healthy animals.

The age wise distribution of canine cases suffering from reactive hepatic disorders and Diabetes mellitus is listed below in Table 3. The dogs suffering from diabetic hepatopathy were in the age group of 4 – 14 years with maximum incidence in 6-8 years of age.

The mean values of haematological parameters in dogs with diabetic hepatopathy are presented below in Table 4. The haematological parameters in affected dogs varied non significantly compared to healthy animals except MCV and MCH which increased significantly. These findings are in accordance with those observed by (Jena *et al*., 2019). Contrary to this Hiblu *et al*., (2015) observed absolute neutrophilia with moderate left shift and marked toxic changes in neutrophils, microcytic hypochromic anemia with some evidence of regeneration on haematological examination in diabetes induced hepatopathy dogs.

The mean values of biochemical parameters in dogs with diabetic hepatopathy are presented below in Table 5 and Figures 1-5. The mean values of ALT,

Table 2. Mean values of clinical parameters in dogs with Diabetes Mellitus

Parameters	Healthy Control (n=12)	Diabetes mellitus (n=8)
Rectal Temperature (°F)	101.53 ± 0.21	101.36±0.41
Heart rate (per min.)	78.71 ± 2.28	109.33±6.17**
Respiration rate (per min.)	30.42 ± 2.49	28.85±3.57

* Significant at 5% (P<0.05); ** Significant at 1% (P<0.01)

Table 3. Age wise distribution of canine cases suffering from reactive hepatic disorders and Diabetes mellitus

Condition	Age group						Total Males	Total Females	Age Range
	< 2 years	2- <4 years	4- <6 years	6- <8 years	8 - <10 years	> 10 years			
Reactive Hepatitis (n = 54)	28	7	9	6	1	3	42	12	3 Months – 14 years
Diabetes mellitus (n=8)	Nil	Nil	2	4	Nil	2	5	3	4 years - 14 years

AST, ALP, GGT, Glucose, BUN and Creatinine were significantly increased whereas mean values of albumin were significantly decreased compared to healthy animals indicative of altered liver and renal functioning. These findings are in accordance with Hiblu *et al*., (2015) and Jena *et al*., (2019) who observed markedly increased levels of Alkaline phosphatase (ALP), Alanine transaminase (ALT) and Aspartate aminotransferase (AST) in diabetic dogs suggestive of hepatic involvement in Diabetes Mellitus. Diabetic dogs often show increased alkaline phosphatase and Alanine aminotransferase (Jena *et al.,* 2019, Rucinsky *et al.,* 2010, Behrend *et al.,* 2018 and Huang, 2012).

It is found in the present study that there is hyperglycemia in diabetic dogs in comparison to healthy dogs. Regardless of the underlying etiology, diabetic dogs are hyperglycemic and glycosuric. Increased fat mobilization leads to hepatic lipidosis, hepatomegaly, hypercholesterolemia, hypertriglyceridemia, and increased catabolism (Behrend *et al.,* 2018, Rucinsky *et al.,* 2010; Sridhar *et al*., 2005 and Huang, 2012). These increments may reflect mild liver cell damage that is related to decreased blood flow due to dehydration. Alterations in lipid metabolism because of diabetes may also contribute to increases in these liver enzymes.

Diabetic dogs may also be associated with other diseases like hepatic necrosis and hepatic enlargement (Hiblu *et al*., 2015). Serum creatinine and BUN are insignificantly increased in the diabetic dogs, as compared to healthy. Evidence for renal failure in diabetic dogs reveals azotemia, increased serum creatinine and BUN (Huang, 2012 and Jena *et al*., 2019).

Liver enzymes ALT and AST are routinely used to obtain information about the integrity of liver cells and the degree of cell destruction. Furthermore, ALP is used as a marker of cholestasis. Because the degree of liver cell destruction correlates with the elevation of the liver enzymes, the results of this study showed that liver cell destruction is not severe in reactive hepatitis. Given that

Table 4 : Mean values of haematological parameters in dogs with diabetic hepatopathy

Parameters	Healthy Control (n=12)	Diabetes mellitus (n=8)
Hb (g/dL)	13.42 ± 0.41	14.14 ± 1.28
PCV (%)	42.17 ± 1.23	41.92±3.63
TEC ($\times10^{12}$/L)	6.58 ± 0.22	5.95±0.51
TLC ($\times10^{9}$/L)	10.42 ± 0.61	12.10±2.33
N (%)	67.83 ± 1.76	73.50±3.17
L (%)	26.70 ± 2.18	20.38±3.46
M (%)	2.83 ± 0.38	3.55±0.71
E (%)	1.85 ± 0.29	1.72±0.38
B (%)	0.79 ± 0.21	0.86±0.42
MCV (fL)	63.95 ± 0.76	68.92±1.80*
MCH (pg)	20.36 ± 0.41	22.74±0.86*
MCHC(g/dL)	32.03 ± 0.69	32.88±0.64
Platelets ($\times10^{9}$/L)	304.70 ± 21.37	346.80±62.32

* Significant at 5% (P<0.05); ** Significant at 1% (P<0.01)

Table 5. Mean values of plasma biochemical parameters in dogs with diabetic hepatopathy

Parameters	Healthy Control (n=12)	Diabetes mellitus (n=8)
ALT (U/L)	24.77 ± 3.83	158.54 ±**20.11****
AST (U/L)	33.04 ± 3.69	113.36 ± 13.19**
ALP (U/L)	62.75 ± 6.18	335.93 ± 39.04**
GGT (U/L)	2.65 ± 0.48	9.30 ± 2.15*
Total Protein (g/dL)	6.59 ± 0.23	5.85 ± 0.36
Albumin (g/dL)	3.55 ± 0.20	2.76 ± 0.28*
Globulin (g/dL)	3.04 ± 0.28	3.09 ± 0.19
A/G ratio	1.22 ± 0.17	0.89 ± 0.12
Total Bilirubin (mg/dL)	0.39 ± 0.07	0.72 ± 0.24
Direct bilirubin (mg/dL)	0.15 ± 0.03	0.31 ± 0.11
Indirect bilirubin (mg/dL)	0.24 ± 0.05	0.42 ± 0.16
Glucose (mg/dL)	93.91 ± 3.83	501.28 ± 41.10**
BUN (mg/dL)	17.56 ± 1.31	42.76 ± 5.87**
Creatinine (mg/dL)	0.82 ± 0.08	1.93 ± 0.19**

* Significant at 5% (P<0.05); **Significant at 1% (P<0.01)

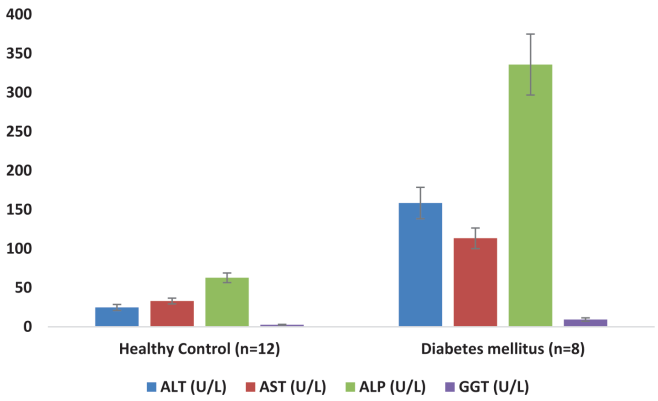

Fig. 1. Plasma levels of liver enzymes in diabetic dogs

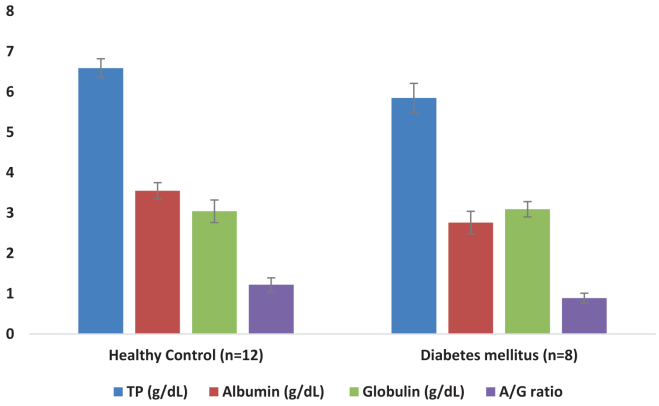

Fig. 2. Plasma Protein levels in diabetic dogs

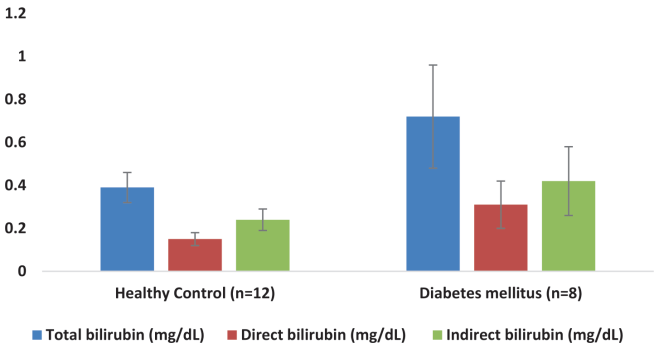

Fig. 3. Plasma Bilirubin levels in diabetic dogs

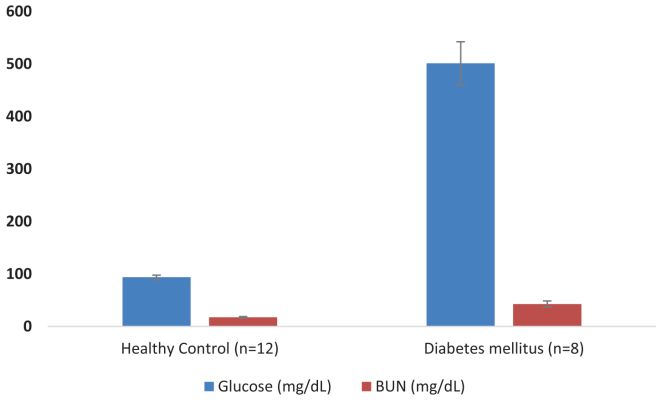

Fig. 4. Plasma Glucose and BUN levels in diabetic dogs

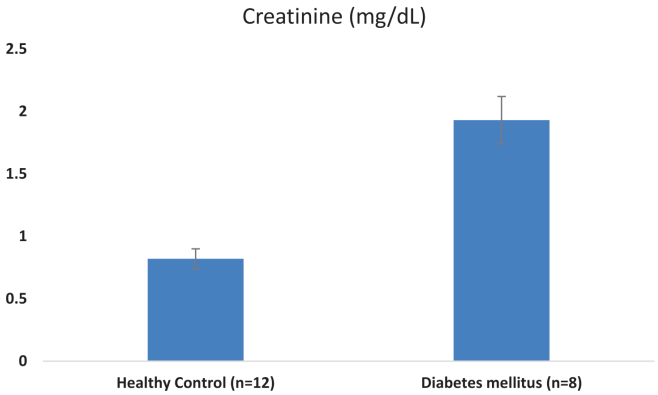

Fig. 5. Plasma Creatinine levels in diabetic dogs

ALP is a marker for cholestasis, we can conclude that reactive hepatitis is not associated with cholestasis in many cases. This is plausible because disturbance of the architecture of the organ, which may cause cholestasis, fails to occur in many cases of reactive hepatitis including diabetes mellitus.

Reactive hepatitis has been found to be associated with disorders of many other organs apart from the liver. Gastrointestinal diseases, heart failure, diseases of the urinary and reproductive system, especially endometritis, were associated more frequently with reactive hepatitis. Apart from this, neoplasia, haemoprotozoan/ rickettsial diseases and endocrine diseases specially Diabetes Mellitus has also been reported to cause reactive hepatopathy in dogs.

In conclusion, the results of our study depicted Diabetes Mellitus as an important cause of reactive hepatitis in dogs and that for diabetic dogs liver enzymes should invariably be measured so as to assess the effect of Diabetes mellitus on Liver which further can help in timely management so as to avoid the hepatopathic effects of this endocrinal disorder.

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