DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF DIABETES MELLITUS IN CANINE

THESIS

Submitted
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MASTER OF VETERINARY SCIENCE

IN

VETERINARY CLINICAL MEDICINE, ETHICS AND JURISPRUDENCE

BY

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I hereby declare that the experimental research work and interpretation of the thesis entitled **DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF DIABETES MELLITUS IN CANINE** or part thereof has not been submitted for any other degree or diploma of any University, nor the data have been derived from any thesis/publication of any University or scientific organization. The sources of materials used and all assistance received during the course of investigation have been duly acknowledged.

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LIST OF ABBREVIATIONS

	Abbreviations		Name
1.	%	:	Percent
2.	α	:	Alpha
3.	@	:	At the rate of
4.	DM	:	Diabetes Mellitus
5.	mg/dl	:	Miligram per deciliter
6.	bid	:	*bis in die*
7.	B Wt	:	Body weight
8.	CBC	:	Complete Blood Count
9.	CDU	:	Color Doppler Ultrasonography
10.	IU	:	International unit
11.	Kg	:	Kilogram
12.	DLC	:	Differential Leucocyte Count
13.	i/m	:	Intra muscular
14.	ml	:	Milliliter
15.	EDTA	:	Ethylene diamine tetra acetic acid
16.	hrs	:	Hours
17.	*et al.*	:	Et alia (and others)
18.	PU	:	Polyuria
19.	g	:	Grams
20.	i.e	:	That is

21.	IV	:	Intravenous
22.	MHz	:	Mega hertz
23.	PD	:	Polydipsia
24.	PU	:	Polyuria
25.	PP	:	Polyphagia
26.	No.	:	Numbers
27.	mg/ml	:	Milligram per milliliters
28.	PO	:	Per Oral
29.	qid	:	quater in die
30.	SC	:	Subcutaneous
31.	SD	:	Standard Deviation
32.	TVCC	:	Teaching Veterinary Clinical Complex
33.	U/L	:	Unit per litre
34.	viz.	:	Namely
35.	WBC	:	White blood corpuscles
36.	BUN	:	Blood Urea Nitrogen
37	VLDL	:	Very Low-Density Lipoprotein
38	HDL	:	High- Density Lipoprotein
39	LDL	:	Low Density Lipoprotein
40.	DKA	:	Diabetic Ketoacidosis
41.	IDDM	:	Insulin- Dependent Diabetes Mellitus
42.	NIDDM	:	Non-Insulin-Dependent Diabetes Mellitus

INTRODUCTION

Diabetes mellitus constitutes the most important global public health problem in humans, and is also of concern in dogs. In developed nations, people and small companion animals share, to varying degrees, their lifestyle and environment. This partnership comes with frequent implications for health and well-being, including high rates of type2 diabetes mellitus, cardiovascular disease and certain cancers. Although diabetes mellitus is considered to be a common endocrine disorder in dogs, its underlying disease mechanisms are poorly understood. Diabetes Mellitus (DM) is not a single disease, but a syndrome characterized by hyperglycemia that result from defects in insulin secretion or insulin sensitivity in target tissues or both. The true incidence of diabetes among cats and dogs is unknown, but experts believe that it is increasing because of the obesity, epidemic and the longer lifespan of cats and dogs. The estimated incidence of obesity among dogs is 22% to 40%, according to a review from the University of Liverpool (German 2006).

Diabetes mellitus (DM) is a treatable condition that requires a committed effort by veterinarian and client. In both dogs and cats, DM is caused by loss or dysfunction of pancreatic beta cells. In the dogs, beta cells loss tend to be rapid and progressive, and it is usually due to immune-mediated destruction, vacuolar degeneration, or pancreatitis (Davison *et al*.,2003). Intact females may be transiently diabetic due to the insulin-resistant effects of the diestrus phase. In cats, loss or dysfunction of beta cells is the result of insulin resistance, islet amyloidosis, or chronic lymphoplasmacytic pancreatitis (Goossens *et al.* 1998) Risk factors for both dogs and cats include insulin resistance caused by obesity, other diseases (e.g., acromegaly in cats, hyper adrenocorticism in dogs), or medications (e.g., steroids, progestins). Genetics is a suspected risk factor, and certain breeds of dogs like Australian terriers, Beagles, Samoyeds, Keeshonden (Hess *et al*.2000) and Burmese cats are more susceptible (Rand *et al*.1997). Regardless of the underlying etiology, diabetic dogs and cats are hyperglycemic and glycosuric, that leads to the classic clinical signs of polyuria, polydipsia (PU/PD), polyphagia, and weight loss. Increased fat mobilization leads to hepatic lipidosis, hepatomegaly, hypercholesterolemia, hypertriglyceridemia, and increased catabolism. In due course hyperketonemia, ketonuria, and ketoacidosis develop and result in progressive compromise of the animal.

Additional signs include lethargy, weakness, and poor body condition as well as cataracts in dogs and peripheral neuropathy in cats. Some animals develop diabetic ketoacidosis with anorexia, dehydration and vomiting.

Even with the advances in diabetic care, diabetes in pets has remained a particular point of interest and discussion among veterinary professionals.

Regardless of cause, deficiency in insulin or its action on target tissues leads to a myriad of abnormalities in carbohydrate, fat and protein metabolism.

Accurately diagnosing and classifying diabetic dogs and cats by knowing the underlying disease process is essential for current and future studies on treatment methods, early detection, treatment of underlying disease, and prevention.

The most common form of diabetes in companion animals varies with the species. Type 1 diabetes mellitus, previously called insulin dependent diabetes, is most common in dogs, whereas type 2, previously called non-insulin–dependent or adult-onset diabetes, appears to be the most common form of diabetes in cats. Other specific types of diabetes account for a smaller proportion of cases in each species. Gestational diabetes has not been reported in cats, but dogs appear to develop an equivalent form during diestrus. The genetic and environmental influences vary with species and the type of diabetes.

Diagnosis is based on clinical signs and persistent glycosuria and hyperglycemia—more than 200 mg/dL for dogs and 250 mg/dL for cats, according to 2010 Diabetes guidelines issued by the American Animal Hospital Association (Rucinsky*et.al*. 2010).

The management of DM in dogs is based on a combination of insulin replacement therapy, diet modification and exercise, designed to maintain near normal blood glucose concentration and minimize fluctuations therein (Maskell and Graham, 1994).Successful insulin therapy and diabetes control require consistent timing, accurate dosing, and careful monitoring, which rely heavily on pet owner participation.

Hence, the investigation was therefore planned to assess the hyperglycaemic conditions in dogs in detail keeping the following objectives in view-

1. To record the prevalence of Diabetes Mellitus in dogs.
2. To study clinico-heamato-biochemical alterations in dogs suffering from Diabetes Mellitus.
3. To evaluate therapeutics modalities in dogs suffering from Diabetes Mellitus.

REVIEW OF LITERATURE

The diabetes mellitus is reported to be the common condition in dogs. However, the clinical features are not very specific and the symptoms exhibited mostly go unnoticed. The exact incidence and severity in canine population is not very clear. Therefore the study was planned to evaluate the incidence and therapeutic measures diabetes mellitus. The work done in the past by several researchers is reviewed as under with appropriate sub heads.

2.1 Prevalence

Guptill *et al.* (2003) reported that the prevalence of diabetes mellitus in dogs presented to veterinary teaching hospitals increased from 19 cases per 10,000 admissions per year in 1970 to 64 cases per 10,000 in 1999, while the case-fatality rate decreased from 37% to 5%. The hospital prevalence of diabetes mellitus was consistently more in older dogs as compared to younger dogs with the highest prevalence occurring in dogs of 10–15 years of age. They also reported an increased risk of diabetes mellitus much more in female dogs as compared to males.

Davison *et al.* (2005) analyzed blood samples of 253 dogs with naturally occurring diabetes mellitus and observed that Labrador retrievers, collies, Yorkshire terriers or crossbred more affected and the age ranges between five and 12 years.

Klinkenberg *et al.* (2006) observed the effect of urbanization of human population and engagement in occupations which leads to change in lifestyle of even the pet dogs. Further they reported that more dependency on commercial pet food and lack of exercise predisposes the urban canine population to diabetes mellitus.

Catchpole *et al.* (2008) reported 0.0005 and 1.5 percent prevalence of canine diabetes in insured pet dogs from United Kingdom. The increase incidence of diabetes mellitus was observed in dogs aged within 5 - 12 years. They classified canine diabetes mellitus into insulin deficiency diabetes (IDD) with absolute insulin deficiency and insulin resistance diabetes (IRD) with relative insulin deficiency. IRD can

complicate and progress to secondary IDD as an outcome of β cell loss in pancreas associated with uncontrolled hyperglycaemia.

Fall (2009) reported 0.3 % to 1.3 % prevalence and seasonal predisposition of diabetes mellitus in canines. The cases of diabetes mellitus were reported at its peak in winter season. Whereas, in other studies there was no seasonal predisposition observed. Breeds that were reported to have a high incidence of diabetes were Samoyed, Cairn Terrier and Australian Terrier, whereas low incidence was seen in Golden Retriever, Boxer and German shepherd.

Huang (2012) reported 0.13 to 0.64 percent incidence of diabetes mellitus in canines affected with multifactorial etiology of β-cell loss, which includes autoimmunity, genetic invariability, environment and diseases resulting in insulin antagonism. Furthermore, he observed a potential immune-mediated cause in diabetes mellitus.

Mattin *et al.* (2014) reported 0.34 percent incidence of canine diabetes mellitus in four-hundred and thirty-nine cases. Out of these, neutered males were at an increased risk of diabetes compared to entire males, whereas neutering was not associated with diabetes in females. The increased risk of canine diabetes mellitus was reported in Yorkshire terriers compared to crossbred dogs, whereas German shepherd dogs and Golden retrievers had lower odds of diabetes mellitus.

Kumar *et al.* (2014) screened 251 dogs of different breeds and reported 10.88 percent incidence of diabetes at Indian Veterinary Research Institute, Izatnagar. Diabetes was confirmed on the basis of random blood sugar and relevant clinical parameters.

Das and Lodh (2015) reported prevalence of diabetes mellitus in canine in and around Kolkata, West Bengal. A total number of 800 clinical cases were screened of which 15 (1.8%) were found positive for diabetes mellitus. Season wise prevalence was highest in the winter (2.20%) and lowest in summer (1.38%). Among different age groups, 7 to 9 years age group was found to be more affected (46.7%), followed by 9 to 12 years (33.3%), 4 to 6 years (20%) and 0 to 3 years age (0%). The breed-wise highest prevalence was reported in Spitz (3.53%) followed by Dachshund (3.33%) whereas, sex wise prevalence was 73.3% in females.

Banfield State Hospital (2016) reported that the prevalence of diabetes mellitus in dogs increased from 13.1 cases per 10,000 in 2006 to 23.6 cases per 10,000 in 2015 with an age ranging from 4-14 years and a peak incidence at 7-9 years. It was reported that the females were twice more likely to develop diabetes than males.

Shruthi *et al.* (2017) observed 0.14% epidemiological incidence of diabetes in dog. Highest incidence was recorded in the age group of 6-9 years in female intact Labrador breeds. Also the highest incidence of diabetes was observed in the month of November and January suggesting a winter predisposition for the disease. Canine diabetes remains a common endocrine disease affecting from one in 100 to one in 500 dogs.

2.2 Clinical signs

Feldman and Nelson (1996) mentioned that diabetes mellitus is one of the common metabolic disorders affecting middle-aged to geriatric dogs characterized by hyperglycaemia, glycosuria and weight loss, resulting from absolute or relative deficiency of insulin. They reported that classification of diabetes mellitus is based on its aetiology and clinical presentation. DM in dog can be classified as either Type 1 or Type 2. Most dogs suffer from Type 1 diabetes in which there is lack of insulin production and dependency on external insulin for survival. In Type 2, insulin production is impaired along with an inadequate response to the hormone.

Hess *et al.* (2000) explained the breed-related differences in diabetes susceptibility and suggested that the pathogenesis of diabetes is influenced by genetic factors and similarities between canine and human diabetes phenotypes indicating the same genes and/or genetic pathways that might be involved in both species.

Catchpole *et al*. (2005) observed polydipsia, polyuria, polyphagia and weight loss in diabetes mellitus in dogs and initial signs of diabetes remain unnoticed, however anorexia, lethargy, vomiting and dehydration may be observed in canine diabetes mellitus.

Huang (2012) reported hyperadrenocorticism obesity, inactivity, cushing's disease in diabetes mellitus. He also observed increased risk of diabetes mellitus in certain breeds, females and neutered males.

Deborah (2015) observed polydipsia as the most common clinical sign of diabetes mellitus in dogs (93%) whereas, polyuria in only 77% of dogs. Also, the weight loss was observed more commonly in dogs (62%) and19% of dogs exhibited polyphagia as a clinical sign of diabetes mellitus. Bilateral cataract formation and acute onset of blindness was observed in approximately 40% diabetic dogs.

Qadri *et al.* (2015) diagnosed diabetes mellitus by the presence of the typical clinical signs like excess thirst, excess urination, excess appetite, and weight loss as well as the presence of a persistently high level of glucose in the blood stream, and the presence of glucose in the urine.

Bruyette (2017) observed insidious onset of diabetes in dogs. The clinical course is chronic in nature which includes polydipsia, polyuria, polyphagia with weight loss, bilateral cataracts, and weakness. Rarely, the infection may cause emphysema due to glucose fermenting organisms such as *Proteus sp., Aerobacteraerogenes*, and *E. coli* and that emphysema may develop in the wall of the gallbladder in diabetic dogs. Hepatomegaly due to lipid accumulation was also recorded in diabetes mellitus cases.

Nerhagen and Mooney (2017) observed polyuria and polydipsia, weight loss, development of bilateral cataracts and lethargy in dogs suffering from diabetes mellitus. Furthermore, they observed that the elevated glucose concentration increases renal tubular threshold which causes osmotic diuresis ultimately resulting in polyuria and polydipsia.

2.3 Factors contributing to increase incidence of Diabetes mellitus

Pathophysiology

Type 1 DM

Al Homsi *et al.* (1992) observed type 1 diabetes with autoimmune destruction of insulin producing cells in the pancreas by CD4+ and CD8+ T cells and macrophages infiltrating the islets.

Holt (2004) described autoimmune destruction of pancreatic β-cells which leads to deficiency of insulin secretion and results in the metabolic derangements associated with T1DM. In addition to the loss of insulin secretion, the function of pancreatic α-cells is also abnormal and there is excessive secretion of glucagons in T1DM patients. Normally, hyperglycemia leads to reduced glucagons secretion; however, in patients with T1DM, glucagons secretion is not suppressed by hyperglycemia. The resultant inappropriately elevated glucagons levels exacerbate the metabolic defects due to insulin deficiency.

He further quoted that insulin deficiency is the primary defect in T1DM, there is also a defect in the administration of insulin. Deficiency in insulin leads to uncontrolled lipolysis and elevated levels of free fatty acids in the plasma, which suppresses glucose metabolism in peripheral tissues such as skeletal muscle. This impairs glucose utilization and insulin deficiency also decreases the expression of a number of genes necessary for target tissues to respond normally to insulin such as glucokinase in liver and the GLUT 4 class of glucose transporters in adipose tissue which explained the major metabolic derangements which result from insulin deficiency in T1DM such as impaired glucose, lipid and protein metabolism.

Catchpole *et al.* (2008) studied insulin deficient diabetes in dogs caused by auto-immune-mediated destruction of β cells. In insulin deficient diabetic dogs, there is no increase in insulin or C-peptide by stimulation of β cells of pancreas located in islets of Langerhans with glucose or glucagon which is suggestive of the unresponsiveness of β-cells.

Benjamin (2010) reported that the diabetes mellitus is a hormonal disorder which exhibit variety of symptoms such as polydipsia, polyuria, polyphagia. polyuria is due to strong osmotic activity of glucose in the distal tubules of the kidneys does not allow water to be removed normally, and diuresis occur.

Feldmen (1983) noted that the glycosuria creates an osmotic diuresis, causing polyuria and, thus, obligatory polydipsia. The author expressed that the polyphagia was because the body is literally starving inspite of hyperglycemia. In response to starvation caused by insulin deficiency, fat and muscle enter a catabolic state to provide energy for needy tissue.

Raju and Raju (2010) stated that 85% of patients have circulating islet cell antibodies and the majorities also have detectable anti-insulin antibodies before receiving insulin therapy. They also reported that most islet cell antibodies are directed against glutamic acid decarboxylase within pancreatic B cells.

Deborah (2015) studied dogs suffering from diabetes mellitus in which infiltrating mononuclear cells and predominantly lymphocytes were observed in 6 of 13 dogs (46%) with diabetes while in 5 of 18 dogs (28%), extensive pancreatic damage appeared to be responsible for the development of diabetes mellitus.

Type 2 DM

Mahler and Adler (1999) reported that insulin resistance and hyperinsulinemia eventually lead to impaired glucose tolerance.

Kumar and Clarke (2002) observed that intimate relationship between the secretion of insulin and sensitivity of hormone action in the complicated control of glucose homeostasis. It is practically impossible to separate the contribution of each to the etio-pathogenesis of DM2.

Anonymous, 2010 in type 2 diabetes impaired insulin secretion through a dysfunction of the pancreatic β-cell and impaired insulin action through insulin resistance was observed in canine diabetes mellitus. The plasma insulin concentration (both fasting and post meal) usually increased, though the severity of insulin resistance and plasma insulin concentration determined to be insufficient to maintain normal glucose homeostasis

2.4 Hemato-biochemical alterations in Diabetes

2.4.1Complete blood count (CBC)

Chung *et al.* (2005) investigated that the peripheral lymphocyte count was inversely related to the severity of diabetic nephropathy. However, they observed that the mechanism for decrease in lymphocyte counts in diabetic nephropathy or cardiovascular disease is still largely unknown.

Deborah (2015) studied common clinico-pathologic features of diabetes mellitus in dogs which include fasting hyperglycemia, hypercholesterolemia, increased liver enzymes (ALP, ALT), neutrophilic leukocytosis, proteinuria, increased urine specific gravity and glycosuria.

Abakpa *et al.* (2017) observed non-significant decrease in packed cell volume, red blood cell count and hemoglobin concentration in alloxan-induced diabetic dogs and increase in white blood cells count. They also noticed higher platelet count and significant increase ($P<0.05$) in creatinine, urea, alanine aminotransferase and aspartate aminotransferase levels in diabetic groups compared to non-diabetic.

Shruthi *et al.* (2017) observed non-significant difference between healthy and diabetic group in respect to parameters like TEC, platelet count, hemoglobin and packed cell volume. They also observed significant increase in serum biochemical parameters like ALT, cholesterol, triglycerides, fasting blood sugar and glycated haemoglobin. However, non-significant increase in the creatinine values was found in the diabetic group as compared to diabetic dogs with mild leukocytosis.

2.4.2 Blood glucose

Qadri *et al.* (2015) mentioned the normal level of glucose in the blood as 80-120 mg/dl (4.4-6.6 mmol/l) which may rise to 250-300 mg/dl (13.6-16.5 mmol/l) following a large or high-calorie meal. They also stated that diabetes is the only common disease that will cause the blood glucose level to rise above 400 mg/dl (22 mmol/l) but some diabetic dogs have a glucose level as high as 700 - 800 mg/dl (44 mmol/l), although most will be in the range of 400-600 mg/dl (22-33 mmol/l). The increase level of blood sugar above 180 mg/dl causes excretion of excess glucose in urine.

2.4.3 Glycated Haemoglobin-

Haberer and Reusch (1998) determined the reference range of glycated haemoglobin for healthy and diabetic dog varying between 2.3 - 4.3% and 4.5 - 8.6%.

Comazzi *et al.* (2008) observed significantly higher concentration of sorbitol in erythrocytes of diabetic dogs with ketonuria.

Sako *et al.* (2008) suggested serum glycated albumin (GA) as an alternative to fructosamine and reported to be useful diagnostic indicator to monitor glycemic control in diabetic dogs.

Kumar *et al.* (2014) reported that fructosamine has an advantage over GHb. The administration of fructosamine reflected glycemic control over the past 2-3 weeks while GHb reflected the same for past 6-8 weeks. Serum fructosamine can also guide in differentiating primary renal glycosuria and Fanconi syndrome in dogs.

Shruthi *et al.* (2017) studied hemato-biochemical alterations in canine diabetes mellitus with special reference to glycatedhaemoglobin and found that the mean concentration of the glycated hemoglobin in healthy dogs was 6.78 ± 0.25% and found to be significantly elevated in the diabetic dogs 9.94 ± 0.42 % with values ranging from 8.6 to 14.2 %. Glucose and glycated hemoglobin values were significantly elevated in diabetic dogs and showed positive correlation on linear regression. Thus, they observed that HbA1c can be considered as one of the important screening test for diabetes mellitus in dogs.

2.4.4 Diabetic nephropathy:

Mongessen (1976) suggested that diabetic nephropathy can be divided into five stages: 1) early hypertrophy stage characterized by increase in renal plasma flow and GFR; 2) silent stage, which is associated with subtle morphological changes, including thickening of the glomerular basement membrane, glomerular hypertrophy, mesangial, and tubulointerstitial expansion; 3) incipient DN characterized by microalbuminuria with likely onset of hypertension; 4) overt DN characterized by dip-stick positive proteinuria; and 5) end-stage renal disease.

Anonymous (2007) stated diabetic nephropathy (DN) refers to a characteristic set of structural and functional kidney abnormalities in patients with diabetes. Diabetes is the most common cause of kidney failure, accounting for nearly 44 percent of new cases.

Dabla (2010) postulated that Cystatin-C may be the preferred marker of diabetic nephropathy in future due to differences in measurements of serum creatinine by various methods. Various studies have shown the importance of measurement of albuminuria, eGFR, serum creatinine and hemoglobin level to further enhance the prediction of end stage renal disease in diabetes mellitus.

2.4.5 Therapeutic regimen-

Kumar *et al.* (2014) suggested insulin therapy, diet modification and exercise along with oral anti-diabetics drugs in canine. They also advised the alternative therapies for the management of canine DM such as gene implants, micro-devices, stem cells and viral based vectors, however these therapies have not yet reached significance for clinical use.

Fall (2009) reported that intact female dogs are usually spayed shortly after diagnosis of diabetes mellitus, because of the insulin-antagonistic features of the sex hormone progesterone. He also suggested subcutaneous injections of insulin for treatment of potential hyperglycaemic dogs.

Cheta and Trifan (2010) reported that zinc, arginine help to stimulate the secretion of insulin while the lettuce extract helps to reduce gastrointestinal glucose absorption.

Rucnisky *et al.* (2010) recommended a porcine lente product (porcine zinc insulin suspension) for dogs as the main stay of treatment for clinical diabetes mellitus to be administered @ 0.25U/ kg.

Maggiore *et al.* (2012) evaluated the efficacy of recombinant human protamine zinc insulin for treatment of 17 diabetic dogs and explained the daily requirement of insulin administration to control hyperglycemia in DM dogs. The most commonly used insulin preparations for diabetes in dogs include recombinant human neutral protamine Hagedorn (NPH) insulin and purified pork source lente insulin. They

further concluded that rhPZI is more effective in diabetic dogs and can be considered as an alternative treatment in diabetic dogs.

Deborah (2015) suggested the line of treatment for diabetes mellitus which includes intermediate-acting insulin (NPH, Lente), at a starting dose of 0.4-0.5 U/kg to be administered twice daily in dogs, whereas, long acting insulin at the dose rate of at 0.8-0.9U/kg once daily.

Bruyette David (2017) suggested initial injections of insulin @ dose of 0.5 U/kg in two divided doses per day in canine diabetes mellitus. He also recommended that the diet and weight reduction alone will not control the disease, therefore suggested the initial therapy. In case of diabetic ketoacidosis initial treatment is 0.2U/kg body weight followed by hourly administration of 0.1 U/kg insulin. Once the serum glucose is <250 mg/dl, the insulin is administered S/C at 0.25–0.5 U/kg, every 4–6 hr, with careful monitoring of the serum glucose at 1 to 2 hr intervals.

Nerhagen and Mooney (2017) advised insulin therapy with intermediate acting porcine lente insulin (Caninsulin) in divided doses of 12 hours interval in canines. They suggested an initial dose of 0.25-0.5 IU/ kg (depending on degree of hyperglycaemia). They expressed that the dose of insulin should be fixed on the basis of blood glucose concentration. Once the blood glucose concentration remains between 3.5mmol/L and 8.0mmol/L for three consecutive measurements, the fixed dose of insulin is advised.

3. MATERIALS AND METHODS

The study was carried out on diagnostic and therapeutic management of diabetes mellitus in canine at Teaching Veterinary Clinical Complex (TVCC), Nagpur Veterinary College, Nagpur and Department of Veterinary Clinical Medicine, Ethics & Jurisprudence, Nagpur Veterinary College, Maharashtra Animal and Fishery Sciences University, Nagpur – 06, Maharashtra.

3.1 Selection of animal

In the present study the dogs presented to TVCC with an age of 5 years or and above, irrespective of breed and sex were screened for random blood glucose. Those having random blood glucose more than 150mg/dl were incorporated in the study and recently whelped bitches, bitches in oestrus or cases of pseudo-pregnancy were excluded.

3.2 Experimental design

Screened dogs were categorized in two groups comprising of six animals in each group. Group I Dogs with DM were treated with alternate therapy consisting combination of Syrup Activated Zinc, Activated Arginine, Calcium Pantothanate, L carnitine and lettuce extract @ 1 ml / 5 kg body weight. Group II dogs with DM were treated with recombinant insulin, @ 0.5 IU/kg, i/m, after meal at every 12 hrs interval.

3.3 Diagnosis of diabetes mellitus

3.3.1 Clinical examination

The complete clinical examination of the dogs was carried out proceeding with the owner's complaint, history of the patient, signalment of the patient. Further, a thorough clinical examination was undertaken by considering the relevant points like polyuria, polydipsia, polyphagia, obesity and bilateral cataract.

3.4 Haematological estimation

For haematological studies, 2 ml blood was collected from the cephalic vein or saphenous vein in a sterile vial containing anticoagulant EDTA (Ethylene Diamine Tetracetic Acid – 2mg/ml blood) and clot activator vial from each dog.

3.4.1.Random blood glucose(mg/dl)

Serum Glucose was estimated by GOD-PAP method using Star 21 Biochemical Semi-Auto Analyzer.

3.4.2. Complete Blood Count (mg/dl)

Complete Blood Count carried out using Hematology Analyzer (Horiba Make ABX Micros ESV-60) on principle of photometry, numeric integration and electronic impedance variation methods.

3.4.3 Serum Creatinine(mg/dl)

Serum Creatinine was estimated by Jaffe's/kinetic method using Star 21 Biochemical Semi-Auto Analyzer (Tietz, 1964).

3.4.4 Blood Urea Nitrogen (mg/dl)

Blood Urea Nitrogen was estimated by Urea-UV (GLDH/kinetic) method using Star 21 Biochemical Semi-Auto Analyzer (Hallett *and Cook,* 1971).

3.4.5 Serum Cholesterol (mg/dl)

Serum Cholesterol was estimated by CHOD-PAP method using Star 21 Biochemical Semi-Auto Analyzer.

3.5.6 Serum Triglyceride (mg/dl)

Serum Triglyceride was estimated by GPO-TOPS method using Star 21 Biochemical Semi-Auto Analyzer.

3.5 Urine analysis

Spot urine samples were collected either during spontaneous urination by following the necessary precautions. It was then subjected for glycosuria, ketonuria, specific gravity using Clinitek Status Automatic Urine Analyser Machine and microscopic examination.

3.6 Therapeutic study

Group I Dogs with DM treated with alternate therapy consisting combination of Syrup Activated Zinc, Activated Arginine, Calcium Pantothanate, L carnitine and lettuce extract @ 1 ml / 5 kg body weight.

Group II Dogs with DM treated with recombinant insulin, @ 0.5 IU/kg, i/m, after meal at every 12 hrs interval**.**

3.7 Statistical analysis

Observations of various parameters recorded during the experiment period were tabulated and the data was statistically analysed using one way classification and student t-test by Snedecor and Cochran (1994).

RESULT AND DISCUSSIONS

The study was carried out at the Teaching Veterinary Clinical Complex (TVCC) and Department of Veterinary Clinical Medicine, Ethics & Jurisprudence, Nagpur Veterinary College, Nagpur on diagnostic and therapeutic management of diabetes mellitus in canine. The dogs presented at TVCC with symptoms of polyuria, polydipsia, polyphagia and obesity of 5 years or and above, irrespective of breed and sex were screened for random blood glucose. Those having random blood glucose more than 150mg/dl were included in the study and recently whelped bitches, bitches in oestrus or cases of pseudo-pregnancy and pyometra were excluded. Complete clinical examination of the dogs was carried out proceeding with the owner's complaint, history of the patient, signalment of the patient. Further, a thorough clinical examination was undertaken by considering the relevant points like polyuria, polydipsia, polyphagia and obesity. Haemato-biochemical estimations viz. Random blood glucose, Complete Blood Count, Serum Creatinine, Blood Urea Nitrogen and Urine analysis were carried out in each group.

Dogs having blood sugar more than 150mg/dl were divided into two groups comprising of six dogs in each group. Group I dogs were treated with alternate therapy consisting combination of Syrup Activated Zinc, Activated Arginine, Calcium Pantothanate, L carnitine and lettuce extract @ 1 ml / 5 kg body weight. Group II Dogs were treated with recombinant insulin, @ 0.5 IU/kg, i/m, after feeding at every 12 hrs interval.

During the period of study, total 642 dogs were screened having polyuria, polydipsia, polyphagia and obesity. Out of which 12 dogs had random blood glucose more than 150 mg/dl and therefore were considered and evaluated for further haemato-biochemical parameters and urinary parameters. The details of the status of blood glucose, prevalence, clinical signs, haemato-biochemical parameters, urine analysis and therapeutic management undertaken are discussed hereunder.

4.1 Prevalence

Table 1: Prevalence of Diabetes mellitus in dog

Number of suspected dogs examined	Number of dogs with diabetes mellitus	Percentage
642	**12**	**1.86**

In the present study prevalence of Diabetes mellitus is shown in Table.1. A total number of 642 clinical cases were screened during the period of six months with clinical signs comprising of polyuria, polydipsia, polyphagia and obesity. Out of which 12 dogs were suspected for Diabetes mellitus. The prevalence at TVCC, NVC, Nagpur was found to be 1.86 %. The above findings are in accordance with Fracassi *et al.* (2004) who reported 1.33 % of prevalence of Diabetes mellitus in dogs and Nelson and Reusch (2014) accounted hospital prevalence rate of 0.4 to 1.2 %. Whereas Shruthi *et al*. (2017) revealed incidence of Diabetes mellitus to be 0.14 % in dogs.

The highest occurrence was observed in Labrador (58.33 %), followed by Spitz (16.66 %) and 8.33 % each of Dachshund, Mongrel and Golden Retriever respectively. The females (66.66%) found to be more affected as compare to males (33.33%) in the present study. The findings are in agreement with Fracassi *et al.* (2004), Davision *et al*. (2005), Das and Lodh (2015).The relative difference with breed-wise prevalence of diabetes mellitus might be due to distribution of particular breed in the geographical area where the study was carried out. However, it is felt that the study with respect to breed, age and sex and its association with diabetes mellitus needs large population size to substantiate the findings.

The common clinical symptoms like polyuria, polydipsia, polyphagia and obesity (Plate 1), lethargy were observed in the present study. However, one single case of bilateral cataract (Plate 2) and four cases of renal affections were observed. The findings are in accordance with Qadri *et al.* (2015) who diagnosed Diabetes mellitus by the presence of the typical clinical signs i.e. excess thirst, excess urination, excess appetite, and weight loss, in addition the presence of a persistently high level of glucose in the blood stream, and the presence of glucose in the urine.

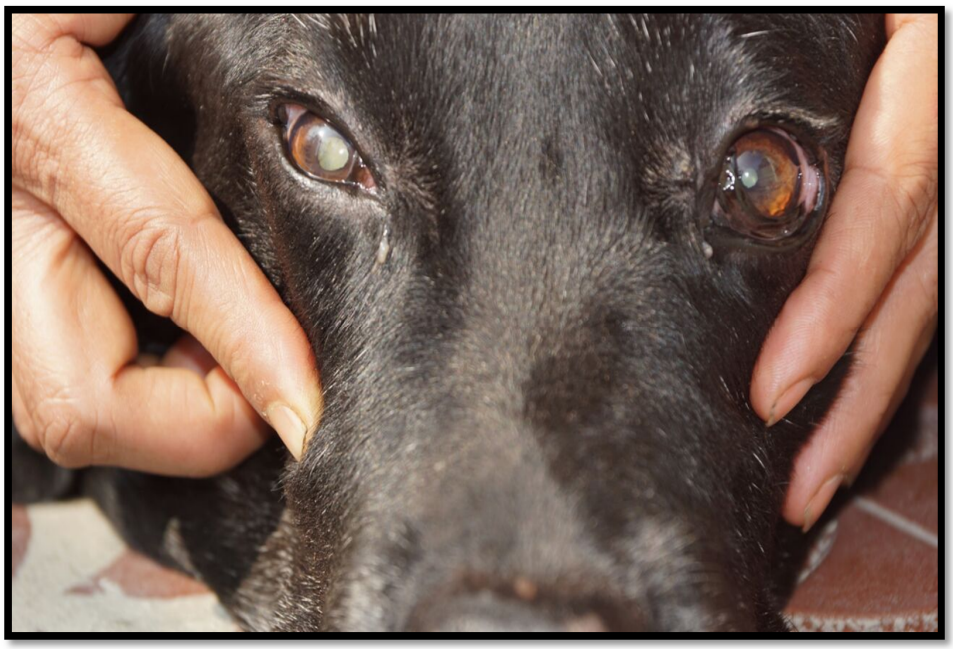


Plate 1: Bilateral cataract in diabetic dog

Plate 2: Diabetes affected dog with obesity

at 7th day, 195.17±25.47 mg/dl in group I whereas 181.67±16.36mg/dl in group II at 14th day of treatment which reduces to 157.50±20.35 mg/dl and 146.00±11.10mg/dl on 21th day of treatment respectively. From the above table it is observed that there is no significant difference between the days as well as between the groups for random blood glucose. It indicates that the random blood glucose does not significantly change during 3rd day to 21th day for both groups.

However, Qadri *et al*. (2015) suggested that blood glucose level may go up to 700-800 mg/dl although most remain in the range of 400-600 mg/dl.

In the present study persistent hyperglycemia was recorded random which may be because of combination of resistance to the actions of insulin in liver and muscle together with impaired pancreatic β-cells function leading to relative insulin deficiency.

However, in susceptible individuals it is likely that pancreatic β-cells are unable to sustain the increased demand for insulin. In the present subject it is likely that the excessive production of glucose in the liver and skeletal muscle result from resistance to the action of insulin.

Medicament of Group I consisted of zinc which is an essential component of many enzymes. Zinc deficiency has been observed secondary to energy metabolism derangement. Another component of this is activated arginine as we know that proteins from main structural components of body cells and an adequate intake is essential for health.

Arginine is a conditionally essential amino acid. However, incorporation of this did not appear to restore post treatment blood glucose level to physiological value.

Fig. 1 : Average Random Blood Glucose in dogs suffering from diabetes mellitus

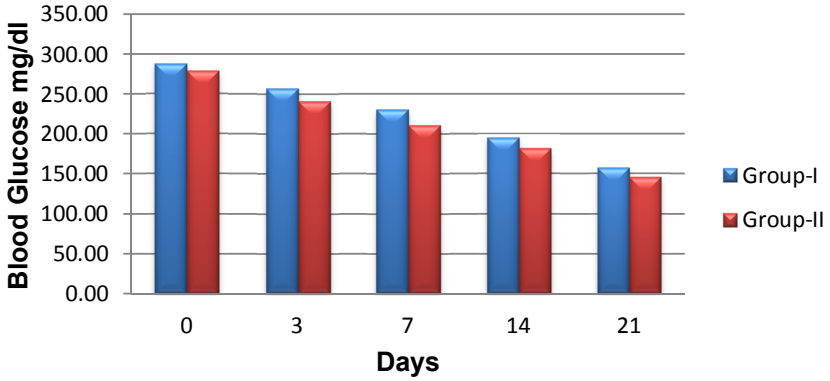


Table 3: Average ± S.E. of Fasting Blood glucose in dogs suffering from diabetes mellitus

Days	0 (mg/dl)	3 (mg/dl)	7 (mg/dl)	14 (mg/dl)	21 (mg/dl)
GROUP-I	248.67 ±44.97	219.17 ±34.41	191.83 ±26.94	166.33 ±23.65	133.67 ±12.96
GROUP-II	230.22 ±17.27	203.50 ±18.65	175.17 ±18.96	147.17 ±11.11	116.83 ±5.59
Result	NS	NS	NS	NS	NS

NS – non significant

Perusal of Table 3 depicts the fasting blood glucose in dogs suspected for diabetes mellitus in both the groups. The average ± S.E. of fasting blood glucose was found to be248.67±44.97 mg/dl in Group-I whereas 230.22±17.27 mg/dl in Group-II at 0^{th} day,219.17±34.41 mg/dl in group-I whereas 203.50±18.65 mg/dl in group-II at 3^{rd} day, 191.83±26.94 mg/dl in group-I whereas 175.17±18.96 mg/dl in group-II at 7^{th} day,166.33±23.65mg/dl in group-I whereas 147.17±11.11 mg/dl in group-II at 14^{th} day, of treatment which reduces 133.67±12.96 mg/dl in group-I whereas 116.83±5.59 mg/dl in group-II at 21^{st} day respectively. In the above table it is recorded that there is no significant difference between the days as well as between the groups. It indicates that the fasting blood glucose does not significantly change during 3 day to 21 days of dogs of both groups. However, variation in blood glucose levels depends on the time of feeding, so it is important to consider the circumstances in which the blood samples were taken. But, in Group-II when compared with the Group-I the values at 21^{st} day are found within the normal reference value. Hence the effectiveness of treatment in Group-II appears to be better. Kumar *et al*. (2014) reported that in insulin treated dogs, concentration of fasting blood sugar vary between 100 and 300 mg/dl which is in accordance with the present findings of the study.

Table 4: Average ± S.E. of Post-Prandial Blood Glucose in dogs suffering from diabetes mellitus

Days	0 (mg/dl)	3 (mg/dl)	7 (mg/dl)	14 (mg/dl)	21 (mg/dl)	CD (1%/5%)
GROUP-I	303.00 ±46.66[a]	252.50 ±35.54[a]	222.50 ±31.16[a]	198.17 ±27.54[b]	160.83 ±16.80[c]	94.25
GROUP-II	289.28 ±7.31 [a]	233.50 ±17.78 [b]	197.17 ±15.74 [c]	178.83 ±10.84 [cd]	149.50 ±5.32 [d]	48.68/35.98
Result	NS	NS	NS	NS	NS	

* = Significant at 5% level, NS – non significant

Different Column-wise superscripts indicates significance

Note:-Rows indicate significance between the different days and it indicates using small alphabet symbol. Column indicates significance between two groups, it indicate using ** (1%) and *(5%) level of significance.

The Average± S.E. of post-prandial blood glucose level. Initially the readings in Group-I was 303.00±46.66, 252.50±35.54, 222.50±31.16, 198.17±27.54 and 160.83±16.80 mg/dl on 0^{th} ,3^{rd},7^{th},14^{th} and 21^{th} day of treatment period where as 289.28±7.31, 233.50±17.78 , 197.17±15.74, 178.83±10.84 and 149.50±5.32 mg/dl on respective days in Group-II. The decreasing trend of post- prandial blood glucose level in both the treatment group was registered. From the above table it is found that there is a significant difference between the days in Group-I. It is observed that post-prandial blood glucose level decreased during 14^{th} to 21^{st} day post treatment significantly; but, the levels did not decrease significantly in first seven days of treatment shown in table no. 4.

Similarly in Group II post-prandial blood glucose level decreased consistently during 3^{rd} to 21^{st} day post treatment, but, did not returned to normal physiological limit.

It can be argued that the regimen adopted in the present study failed to control the desired level of glycaemia control.

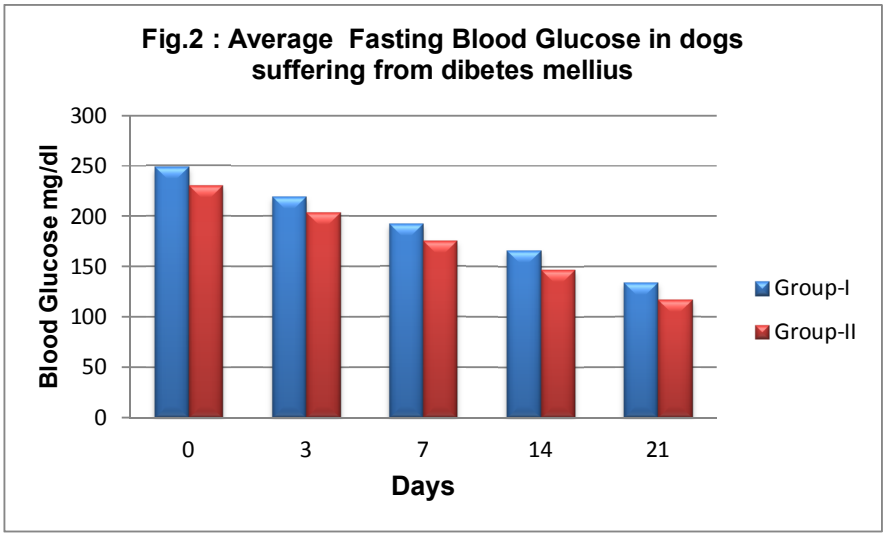


Fig.2 : Average Fasting Blood Glucose in dogs suffering from dibetes mellius
Blood Glucose mg/dl
300
250
200
150
100
50
0
0
3
7
14
21
Days
Group-I
Group-II

Table 5: Average ± S.E. of Cholesterol in dogs suffering from diabetes mellitus

Days	0 (mg/dl)	3 (mg/dl)	7 (mg/dl)	14 (mg/dl)	21 (mg/dl)
GROUP-I	318.50 ±19.72	319.00 ±20.84	323.33 ±22.71	324.50 ±23.12	324.83 ±23.46
GROUP-II	310.83 ±12.22	313.17 ±11.92	315.33 ±12.41	314.50 ±12.02	330.50 ±23.25
Result	NS	NS	NS	NS	NS

NS – non significant

From Table 5 it is observed that the cholesterol level in Group-I increased from 318.50±19.72 to 324.83±23.46mg/dl from 0^{th} day to 21^{st} day of treatment. Similar trend was observed in Group-II the cholesterol level increased from 310.83±12.22 to 330.50±23.25 mg/dl on 21th day of treatment. No significant difference in cholesterol level between the days as well as between the groups was recorded. The observed values at 0^{th} day in both the group are much more than the normal reference range i.e.125 – 250 mg/dl (Benjamin, 2010). When there is deficiency of insulin, glucose uptake is impaired and this excess glucose is converted to cholesterol.(Feldman, 1983) cited that in diabetes, the plasma cholesterol concentration is usually elevated, and this may play a role in the accelerated development of the arteriosclerotic vascular disease, which is a major long-term complication of diabetes in humans. Part of rise in plasma cholesterol is due to an increase in the cholesterol containing very low-density and very low-density beta-lipoprotein secondary to the great increase in circulating triglycerides. Another factor may be decline in hepatic degradation of cholesterol (Ganong, 1979).

Table 6: Average ± S.E. of Triglyceride in dogs suffering from diabetes mellitus

Days	0(mg/dl)	3(mg/dl)	7(mg/dl)	14(mg/dl)	21(mg/dl)
GROUP-I	162.67 ±7.54	161.67 ±7.74	163.17 ±7.12	165.00 ±7.74	163.17 ±8.18
GROUP-II	163.50± 9.08	166.83 ±9.27	165.33 ±8.56	167.33 ±8.07	165.33 ±7.33
Result	NS	NS	NS	NS	NS

NS – non significant

Fig. 3: Average Post-prandial Blood Glucose in dogs suffering from diabetes mellitus

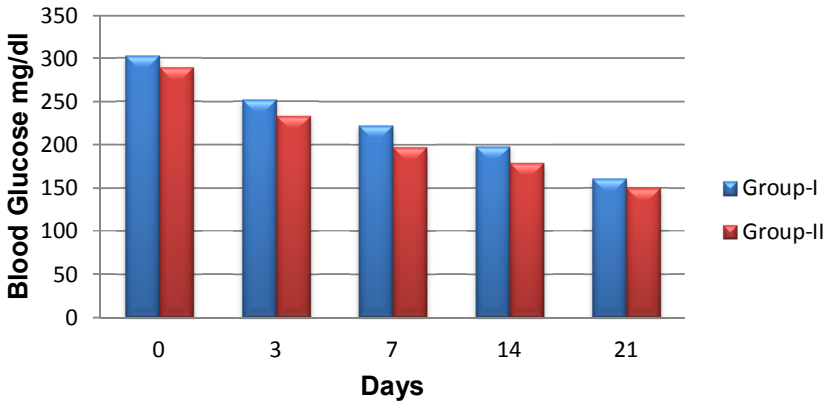


Table 5: Average ± S.E. of Cholesterol in dogs suffering from diabetes mellitus

Days	0 (mg/dl)	3 (mg/dl)	7 (mg/dl)	14 (mg/dl)	21 (mg/dl)
GROUP-I	318.50 ±19.72	319.00 ±20.84	323.33 ±22.71	324.50 ±23.12	324.83 ±23.46
GROUP-II	310.83 ±12.22	313.17 ±11.92	315.33 ±12.41	314.50 ±12.02	330.50 ±23.25
Result	NS	NS	NS	NS	NS

NS – non significant

From Table 5 it is observed that the cholesterol level in Group-I increased from 318.50±19.72 to 324.83±23.46mg/dl from 0th day to 21st day of treatment. Similar trend was observed in Group-II the cholesterol level increased from 310.83±12.22 to 330.50±23.25 mg/dl on 21th day of treatment. No significant difference in cholesterol level between the days as well as between the groups was recorded. The observed values at 0th day in both the group are much more than the normal reference range i.e.125 – 250 mg/dl (Benjamin, 2010). When there is deficiency of insulin, glucose uptake is impaired and this excess glucose is converted to cholesterol.(Feldman, 1983) cited that in diabetes, the plasma cholesterol concentration is usually elevated, and this may play a role in the accelerated development of the arteriosclerotic vascular disease, which is a major long-term complication of diabetes in humans. Part of rise in plasma cholesterol is due to an increase in the cholesterol containing very low-density and very low-density beta-lipoprotein secondary to the great increase in circulating triglycerides. Another factor may be decline in hepatic degradation of cholesterol (Ganong, 1979).

Table 6: Average ± S.E. of Triglyceride in dogs suffering from diabetes mellitus

Days	0(mg/dl)	3(mg/dl)	7(mg/dl)	14(mg/dl)	21(mg/dl)
GROUP-I	162.67 ±7.54	161.67 ±7.74	163.17 ±7.12	165.00 ±7.74	163.17 ±8.18
GROUP-II	163.50± 9.08	166.83 ±9.27	165.33 ±8.56	167.33 ±8.07	165.33 ±7.33
Result	NS	NS	NS	NS	NS

NS – non significant

Fig. 4 : Average Cholesterol in dogs suffering from diabetes mellitus

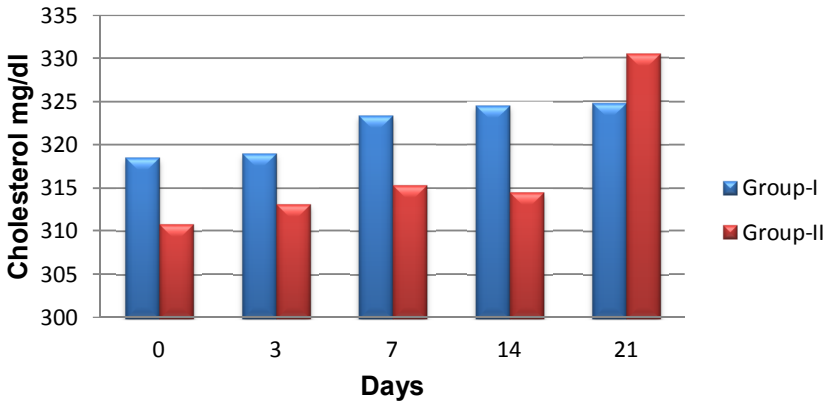
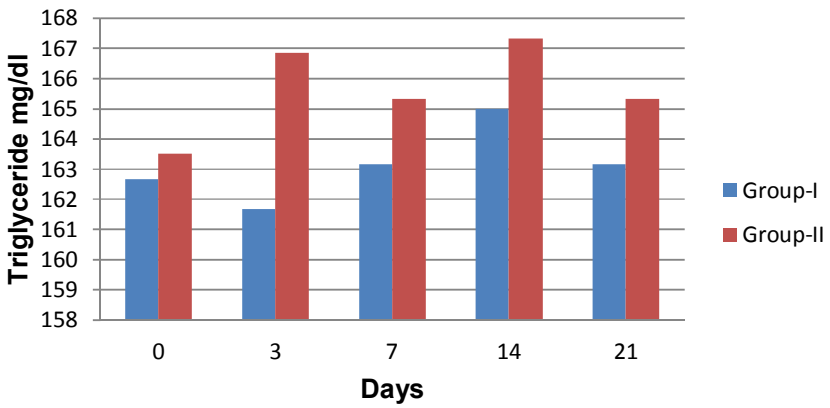


Fig. 5 : Average Triglyceride in dogs suffering from diabetes mellitus



The Average ± S.E. of Triglyceride in affected dogs is presented in Table 6. The observed values in the present study found to be at higher level when compare to the normal reference values i.e.27.43 mg/dl - 114.17 mg/dl (Cohen and Kneiser, 1980). The triglyceride levels slowly get increase from 0^{th} day to 21^{th} day. In Group-I it was 162.67±7.54, 162.67±7.54, 163.17±7.12, 165.00±7.74 and 163.17±8.18 mg/dl respectively and 163.50±9.08, 166.83±9.27, 165.33±8.56, 167.33±8.07 and 165.33±7.33mg/dl respectively. It is found that there is no significant difference between the days as well as between the groups of different days for triglyceride level. Elevated triglyceride levels are also a component of metabolic syndrome and hence in the present study the values are more as compared to the normal reference values.(Feldman, 1983)cited that in uncontrolled diabetes, there is an increase in the plasma concentration of triglycerides, cholesterol, lipoproteins, chylomicrons, and free fatty acids. These factors contribute to the development of lipemic plasma. The rise in these constituents is due mainly to decreased removal of triglycerides into the fat depots. The enzyme lipo-protein lipase aids in the metabolism of very low-density lipoprotein (VLDL) and chylomicrons. Without insulin, lipoprotein lipase fails to be produced and the lipemia mentioned above is produced. With insulin therapy, the triglyceride –rich VLDL and chylomicrons are metabolized and triglyceride concentration will be reduced. Low-density lipoprotein, which is high in cholesterol, is a by-product of chylomicrons metabolism. Therefore, the treated diabetic often is seen to have reducing serum cholesterol concentrations.

Table 7:Average ± S.E. of Blood Urea Nitrogen in dogs suffering from diabetes mellitus

Days	0 (mg/dl)	3 (mg/dl)	7 (mg/dl)	14 (mg/dl)	21 (mg/dl)
GROUP-I	48.13 ±19.99	45.98 ±19.77	45.02 ±19.63	42.95 ±19.08	40.42 ±18.08
GROUP-II	24.15 ±3.76	23.93 ±4.11	23.80 ±3.91	23.33 ±3.65	22.87 ±3.37
Result	NS	NS	NS	NS	NS

NS – non significant

Table 7 depicts the value of Blood Urea Nitrogen in diabetes affected animals. The BUN levels in Group-I is elevated i.e. 48.13±19.99 , 45.98±19.77, 45.02±19.63, 42.95±19.08 and 40.42±18.08 mg/dl as some of the dogs in Group-

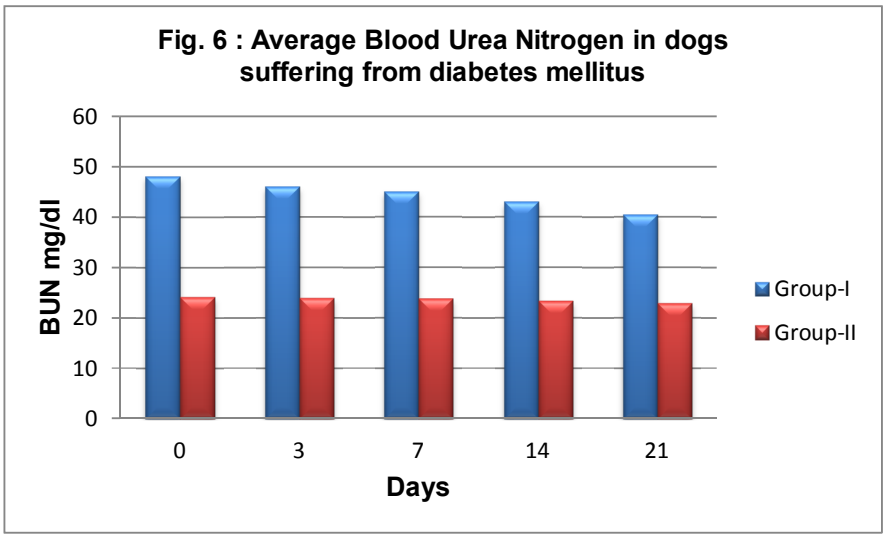


Fig. 6 : Average Blood Urea Nitrogen in dogs suffering from diabetes mellitus
BUN mg/dl
60
50
40
30
20
10
0
0
3
7
14
21
Days
Group-I
Group-II

I were having renal affections where as the values in Group-II found to be in the normal range. It is found that there is no significance difference between the days as well as between the groups of different days for BUN in the present study. It appears that hyperglycemia recorded in both the groups is not sufficiently severe to cause osmotic dieresis so as to cause hemoconcentration associated with renal ischemia.

Table 8:Average ± S.E. of Serum Creatinine in dogs suffering from diabetes mellitus

Days	0 (mg/dl)	3 (mg/dl)	7 (mg/dl)	14 (mg/dl)	21 (mg/dl)
GROUP-I	2.43 ±0.94	2.34 ±0.83	2.12 ±0.68	1.81 ±0.54	1.40 ±0.36
GROUP-II	1.86 ±0.29	1.70 ±0.28	1.51 ±0.25	1.22 ±0.20	1.16 ±0.97
Result	NS	NS	NS	NS	NS

NS – non significant

Perusal of Table 8 depicts the Serum Creatinine level of diabetic affected dogs and similar observations were noted as per the BUN levels .Increase levels were observed in Group-I in first half of treatment period because of the renal affections. The values in both the group at the terminal stages of treatment period found within normal limits.

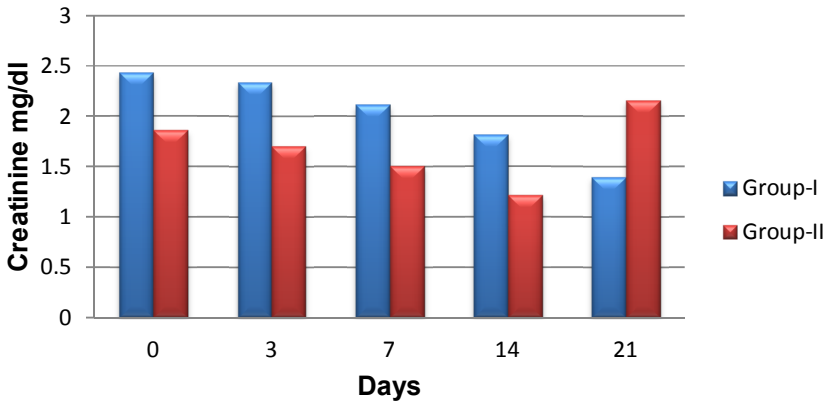
Table 9: Average ± S.E. of Haemoglobin in dogs suffering from diabetes mellitus

Days	0 (gm %)	3 (gm %)	7 (gm%)	14 (gm%)	21 (gm%)
GROUP-I	12.48 ±1.61	12.58 ±1.47	12.78 ±1.52	12.90 ±1.49	12.67 ±1.45
GROUP-II	13.52 ±0.67	13.35 ±0.70	13.83 ±0.64	13.53 ±0.62	13.38 ±0.73
Result	NS	NS	NS	NS	NS

NS – non significant

Table 9 represents the haemoglobin levels in both the groups no significant difference between the days as well as between the groups of different

Fig. 7 : Average Serum Creatinine in dogs suffering from diabetes mellitus



days for haemoglobin was observed. The findings are in agreement with Shruthi *et al.*(2017).

Table 10: Average ± S.E. of Packed Cell Volume in dogs suffering from diabetes mellitus

Days	0 (%)	3 (%)	7 (%)	14 (%)	21 (%)
GROUP-I	36.65 ±4.72	36.63 ±4.69	36.77 ±4.66	36.90 ±4.67	36.95 ±4.63
GROUP-II	41.27 ±1.68	40.77 ±1.79	41.83 ±1.59	41.08 ±1.64	40.80 ±1.65
Result	NS	NS	NS	NS	NS

NS – non significant

No significance difference was noted between the days as well as between the groups for PCV. The PCV is in normal reference values. The findings are in agreement with Shruthi *et al.* (2017).

Table 11: Average ± S.E. of Total Erythrocyte Count in dogs suffering from diabetes mellitus

Days	0 (10^6)	3 (10^6)	7 (10^6)	14 (10^6)	21 (10^6)
GROUP-I	5.53 ±0.57	5.57 ±0.61	5.60 ±0.55	5.69 ±0.54	5.70 ±0.51
GROUP-II	6.85 ±0.38	6.66 ±0.33	6.62 ±0.30	6.54 ±0.27	6.84 ±0.30
Result	NS	NS	NS	NS	NS

NS – non significant

Total Erythrocyte Count of the affected dogs is shown in Table 11which is in normal range and it is found that there is no significance between the days as well as between the groups of different days for TEC. The findings are in agreement with Shruthi *et al.* (2017).

Table 12: Average ± S.E. of Neutrophils in dogs suffering from diabetes mellitus

Days	0 (%)	3 (%)	7 (%)	14 (%)	21 (%)	CD (1%/5%)
GROUP-I	79.33 ±3.07 [a]	77.50 ±2.51 [ab]	77.00 ±2.42 [ab]	72.50 ±1.52 [bc]	69.83 ±1.30 [c]	6.590
GROUP-II	80.33 ±1.98 [a]	79.77 ±1.59 [a]	78.55 ±1.10 [ab]	75.07 ±0.95 [bc]	73.30 ±1.30 [c]	4.162
Result	NS	NS	NS	NS	NS	

* = Significant at 5% level, NS – non significant
Different Column-wise superscripts indicates significance
Note:-Rows indicate significance between the different days and it indicate using small alphabet symbol.
Column indicates significance between two groups, it indicate using **(1%)and *(5%) level of significance.

From Table 12 it is found that there is a significant change between the days. Neutrophills changes from 3rd day, it is decreases upto 7th day and after 14th and 21th days it is significantly decreases in group-I. It also observed that in group-II, neutrophills does not decrease upto 7th day but from 14th day to 21st day decreases significantly which might be due to the secondary bacterial infections and responds to therapy.

Table 13: Average ± S.E. of Lymphocyte in dogs suffering from diabetes mellitus

Days	0 (%)	3 (%)	7 (%)	14 (%)	21 (%)	CD (1%/5%)
GROUP-I	15.83 ±3.22[b]	17.17 ±2.68[b]	18.17 ±2.68[b]	22.33* ±2.08[ab]	26.67 * ±1.65[a]	7.33
GROUP-II	14.57 ±2.06 [c]	16.00 ±1.51 [bc]	16.37 ±1.45 [bc]	19.40* ±1.24 [ab]	22.43* ±1.45 [a]	4.553
Result	NS	NS	NS	Significant	Significant	

* = Significant at 5% level, NS – non significant
Different Column-wise superscripts indicates significance
Note:-Rows indicate significance between the different days and it indicate using small alphabet symbol.
Column indicates significance between two groups, it indicate using **(1%)and *(5%) level of significance.

Significant change in lymphocyte count was observed within different day for group-I Table 12. It found that there is no significant changes on lymphocyte up to 7 days but from day 14 to day 21 it found that lymphocyte increases significantly. In group-II it is observed that lymphocyte significantly increases from 3rd day to 21st day .If we compare two groups for different days, it is found that there is no significant changes between the groups upto 7 days but 14th and 21st day lymphocyte have been change significantly.

Table 14: Average ± S.E. of Eosinophils in dogs suffering from diabetes mellitus

Days	0 (%)	3 (%)	7 (%)	14 (%)	21 (%)
GROUP-I	3.17 ±0.31	3.33 ±0.21	3.17 ±0.17	3.50 ±0.22	2.50 ±0.22
GROUP-II	3.35 ±0.41	3.05 ±0.34	3.57 ±0.46	3.37 ±0.40	3.05 ±0.43
Result	NS	NS	NS	NS	NS

NS – non significant

Table 14 depicts the value of eosinophil count, and it is found that there is no significance difference between the days as well as between the groups of different days for eosinophil. It indicates that the eosinophil does not significantly change during 3 day to 21 days for both groups.

Table 15: Average ± S.E. of Platelets in dogs suffering from diabetes mellitus

Days	0 (10^3/mm^3)	3 (10^3/mm^3)	7 (10^3/mm^3)	14 (10^3/mm^3)	21 (10^3/mm^3)
GROUP-I	328.50 ±69.51	331.83 ±68.69	331.00 ±65.90	332.17 ±64.31	332.83 ±63.79
GROUP-II	406.50 ±62.68	409.50 ±59.25	408.50 ±59.90	406.83 ±57.41	406.83 ±54.81
Result	NS	NS	NS	NS	NS

NS – non significant

No significance difference between the days as well as between the groups of different days for platelet count was observed. It indicate that the platelet does not significantly change during 3 day to 21 days for both groups.

Table 16: Average ± S.E. of Total leukocyte count in dogs suffering from diabetes mellitus

Days	0 (10^3)	3 (10^3)	7 (10^3)	14 (10^3)	21 (10^3)
GROUP-I	11.95 ±2.03	11.60 ±1.87	10.37 ±1.34	9.77 ±1.04	9.12 ±0.86
GROUP-II	11.80 ±1.18	12.05 ±1.13	12.33 ±1.32	11.91 ±1.19	11.65 ±1.06
Result	NS	NS	NS	NS	NS

NS – non significant

From Table 16 it is found that there is no significance difference between the days as well as between the groups of different days for Total leukocyte count was observed. It indicates that the Total leukocyte count does not significantly change during 3 day to 21 days for both groups.

4.3 Urinalysis

The urinary parameters were studied to know the health status of dogs having diabetes affections so as to decide the supportive therapeutic regimen. Out of 12 dogs whose urine was collected, the traces of glucose were found in 100 % cases. Ketone in 33 % cases. Proteinuria was studied and found that in 33.33 per cent cases the severity of proteinuria 2 + and above.

The specific gravity was estimated and it was observed that there was non-significant increase in specific gravity. The urinary specific gravity have important role, though, in the present investigation no significance was observed.

4.4 Bacteriological Examination of Urine:

The isolation and cultural test was carried out to know the pathogen as well as for the therapeutic regimen. Cultural examination of sterile urine samples on specific media revealed the presence *E. coli* in 33.33% samples. No bacterial growth was observed in 66.33% samples. Antibiogram analysis revealed that the microorganism were highly sensitive to different antibiotics viz. Ampicillin, Norfloxacin, Ceftiofur sodium, Nitrofurantoin, enrofloxacin, amoxicillin, ceftriaxone and amikacin.

4.5 Sonography

In animals with clinical signs of diabetes, inability to palpate the pancreas or identify them on survey abdominal radiographs is another indication for ultrasonography. The ultrasound examination in the present investigation was carried out in all the cases using a Toshiba, Just vision 200 ultrasound scanner, with triple frequency transducer having 3.5 - 5.00 MHz convex and 5.0-7.5 MHz linear transducer. The selection of the transducer of appropriate frequency and routine preparations for ultrasound viz. administration of laxative a day prior to examination, wherever possible, cleaning of ventral abdomen, close clipping and application of couplin gel allowed proper visualization of the organ images. Total 12 dogs were scanned for examination of pancreas. Out of these cases, the pancreas could be visualized properly in 9 cases whereas in two cases, gas filled stomach and intestines obstructed the view. The pancreas appeared hyperechoic in 2 cases with uniform echotexture, whereas in 7 cases, the pancreas appeared normal ultrasonographically. Ultrasound examination is a very useful diagnostic modality for identifying various pathologies of the soft tissue organs such as malignancies, cysts, swelling etc. However, in the present investigation, no such abnormalities of pancreas were noted. It was therefore concluded that the ultrasound examination is not a very useful tool for diagnosing the primary diseases like diabetes, unless has some gross abnormalities.

SUMMARY AND CONCLUSIONS

The study entitled “Diagnostic and therapeutic management of diabetes mellitus in canine” was carried out at the Teaching Veterinary Clinical Complex (TVCC) and Department of Veterinary Clinical Medicine, Ethics & Jurisprudence, Nagpur Veterinary College, Nagpur. The dogs presented at TVCC with symptoms of polyuria, polydipsia, polyphagia and obesity of 5 years or and above were screened for random blood glucose. Those having random blood glucose more than 150mg/dl were included in the study. However, recently whelped bitches, bitches in oestrus or cases of pseudo-pregnancy and pyometra were excluded. Complete clinical examination of the dogs was carried out followed by a thorough clinical examination. Haemato-biochemical estimations were carried out in each group.

During the period of study, total 642 dogs showing typical symptoms of diabetes were screened. Out of these cases, 12 dogs had random blood glucose more than 150 mg/dl and therefore were considered and evaluated for further haemato-biochemical parameters and urinary parameters.

5.1 Prevalence

The data revealed the prevalence of 1.86 %. The highest occurrence was observed in Labrador (58.33 %), followed by Spitz (16.66 %) and 8.33 % each of Dachshund, Mongrel and Golden Retriever, respectively. The relative difference with breed-wise prevalence of diabetes mellitus might be due to distribution of particular breed in the geographical area where the study was carried out.

The common clinical symptoms like polyuria, polydipsia, polyphagia and obesity, lethargy were observed in the present study. In one single case, bilateral cataract was noticed whereas in four cases renal affections were noted.

The symptoms were mainly attributed either to the abundance of glucosein the blood or to the shortage of nutrients within cells. The symptoms exhibited by the dogs suffering from diabetes such as polydipsia, polyuria and polyphagia. The glycosuria creates an osmotic diueresis, causing polyuria and thus obligatory polydipsia. The polyphagia occurs because the body is starving inspite of hyperglycemia. In response to this starvation caused by insulin deficiency, fat and muscle enter a catabolic state to provide energy for needy

tissue. The major complaint at first consultation was increased thirst and increased urination. Other symptoms observed were exertion weakness, loss of vision, and infections.

Screened dogs were divided into two groups comprising of six animals in each group. Group I Dogs diabetes mellitus treated with a therapeutic regimen consisting a combination of Syrup Activated Zinc, Activated Arginine, Calcium Pantothanate L carnitine and lettuce extract @ 1 ml / 5 kg body weight. Group II Dogs diabetes mellitus were treated with recombinant insulin, @ 0.5 IU/kg, i/m, after meal at every 12 hrs interval**.** The comparison in both the groups were evaluated as per haemato-biochemical parameters.

5.2Hemato-biochemical parameters

Random Blood Sugar

The average ± S.E. of Random Blood Glucose was found to be287.57±43.97 mg/dl on day 0 in Group-I whereas 278.33±28.93 mg/dl in Group-II which gradually reduced to 157.50±20.35 mg/dl and 146.00±11.10mg/dl on 21th day of treatment, respectively. There was no significant difference between the days as well as between the groups for random blood glucose. It indicated that the random blood glucose does not significantly change during 3rd day to 21th day for both groups.

In the present study persistent hyperglycemia was recorded random which may be because of combination of resistance to the actions of insulin in liver and muscle together with impaired pancreatic β-cells function leading to relative insulin deficiency. However, in susceptible individuals it is likely that pancreatic β-cells are unable to sustain the increased demand for insulin. In the present subject it is likely that the excessive production of glucose in the liver and skeletal muscle result from resistance to the action of insulin.

Medicament of Group I consisted of zinc which is an essential component of many enzymes. Zinc deficiency has been observed secondary to energy metabolism derangement. Another component of this is activated arginine as we know that proteins from main structural components of body cells and an adequate intake is essential for health. Arginine is a conditionally essential amino acid. However, incorporation of this did not appear to restore post treatment blood glucose level to physiological value.

Fasting Blood glucose

The average ± S.E. of Fasting Blood Glucose was found to be248.67±44.97 mg/dl on day 0 in Group-I and 230.22±17.27 mg/dl in Group-II and reduced to 133.67±12.96 mg/dl in group-I and 116.83±5.59 mg/dl in group-II at 21st day, respectively. There was no significant difference between the days as well as between the groups. It indicated that the fastingblood glucose does not significantly change during 3 day to 21 days for both groups. In Group-II when compared with the Group-I, the values at 21st day were found within the normal reference value. Hence the effectiveness of treatment in Group-II appears to be better.

Post-prandial Blood Glucose

The post-prandial blood glucose values in Group-I were 303.00±46.66 on day 0, whereas 160.83±16.80 mg/dl on 0th 21th day of treatment period. Similarly, they were 289.28±7.31 mg/dl on day 0 and 149.50±5.32 mg/dl on day 21 in Group-II. The decreasing trend of post- prandial blood glucose level in both the treatment group was noticed. The difference between the intervals was significant in Group-I after 7th day. Similarly in Group II Post-prandial Blood Glucose level decreased consistently during 3rd to 21st day post treatment, but, did not returned to normal physiological limit.

Serum Cholesterol

The Serum Cholesterol level in Group-I increased from 318.50±19.72 to 324.83±23.46mg/dl from 0th day to 21st day of treatment. Similar trend was observed in Group-II the cholesterol level increased from 310.83±12.22 to 330.50±23.25 mg/dl on 21th day of treatment. However, the differences were non-significant between the intervals and between the groups. The observed values at 0th day in both the group were much higher than the normal reference range i.e.125 – 250 mg/dl.When there is deficiency of insulin, the plasma cholesterol concentration is usually elevated, and this may play a role in the accelerated development of the arteriosclerotic vascular disease, which is a major long-term complication of diabetes.

Serum Triglyceride

The Average ± S.E. of Triglyceride in affected dogs slowly increased from 0^{th} day to 21^{th} day. In Group-I it was162.67±7.54 m/dl on day 0, which showed irregular non-significant trend and the values on day 21 was 163.17±8.18 mg/dl. In Group II, the mean values was 163.50±9.08 and on day 21 165.33±7.33mg/dl. Thus it was observed that there was no significant difference between the days as well as between the groups of different for triglyceride level.

Blood Urea Nitrogen

The BUN levels in Group-I showed increased levels over the normal physiological levels i.e. 48.13±19.99 , 45.98±19.77, 45.02±19.63,42.95±19.08 and 40.42±18.08 mg/dl as some of the dogs in Group-I were having renal affections where as the values in Group-II found to be in the normal range. It is found that there is no significance difference between the days as well as between the groups of different days for BUN in the present study. It appears that hyperglycemia recorded in both the groups is not sufficiently severe to cause osmotic dieresis so as to cause hemoconcentration associated with renal ischemia.

The haematological parameters such as TLC, haemoglobin, PCV and TEC and biochemical parameter serum creatinine, did not show any significant difference within the days and between the groups.

The values of neutrophils indicated that there was a significant difference between the days. The values changed from 3^{rd} day, it is decreases upto 7^{th} day and after 14^{th} and 21th days it is significantly decreases in group-I. It also observed that in group-II, neutrophils did not decrease upto 7^{th} day but from 14^{th} day to 21^{st} day decreased significantly which might be due to the secondary bacterial infections and responds to therapy. Significant change was also observed in lymphocyte count within different day for group-I. It was observed that there was no significant changes on lymphocyte up to 7 days but from day 14 to day 21, the lymphocyte increased significantly. In group-II it was observed that lymphocyte significantly increases from 3^{rd} day to 21^{st} day .If we compare two groups for different days, it was found that there is no significant changes between the groups upto 7 days but 14^{th} and 21^{st} day lymphocyte have been change significantly.

The urinalysis indicated that out of 12 dogs whose urine was collected, the traces of glucose were found in 100 % cases. Ketone in 33 % cases. Proteinuria was studied and found that in 33.33 per cent cases the severity of proteinuria 2 + and above. There was non-significant increase in specific gravity.

The cultural examination of sterile urine samples on specific media revealed the presence *E. coli* in 33.33% samples, whereas no bacterial growth was observed in 66.33% samples. Antibiogram analysis revealed that the microorganism were highly sensitive to different antibiotics viz. Ampicillin, Norfloxacin, Ceftiofur sodium, Nitrofurantoin, enrofloxacin, amoxicillin, ceftriaxone and amikacin.

The ultrasound examination indicated pancreas as hyperechoic in two cases with uniform echotexture (Plate 3), whereas in seven cases, the pancreas appeared normal ultrasonographically. In the present investigation, no such abnormalities of pancreas were noted. It was therefore concluded that the ultrasound examination is not a very useful tool for diagnosing the primary diseases like diabetes, unless has some gross abnormalities.

CONCLUSIONS

From the investigation, following conclusions have been drawn-

1. The prevalence of diabetes mellitus in dogs was found to be 1.86%, more in Labrador breed and females were more affected at TVCC, Nagpur Veterinary College, Nagpur.
2. The common symptoms exhibited by diabetic dogs are polydipsia, polyuria and polyphagia.
3. There was no significant effect of treatment on fasting blood glucose levels, however, the post-prandial blood glucose levels significantly decreased between the intervals.
4. Treatment of diabetic dogs with injections of recombinant insulin @ 0.5 IU/kg, intramuscularly twice a day resulted in significant decrease in blood glucose levels over the period of time.

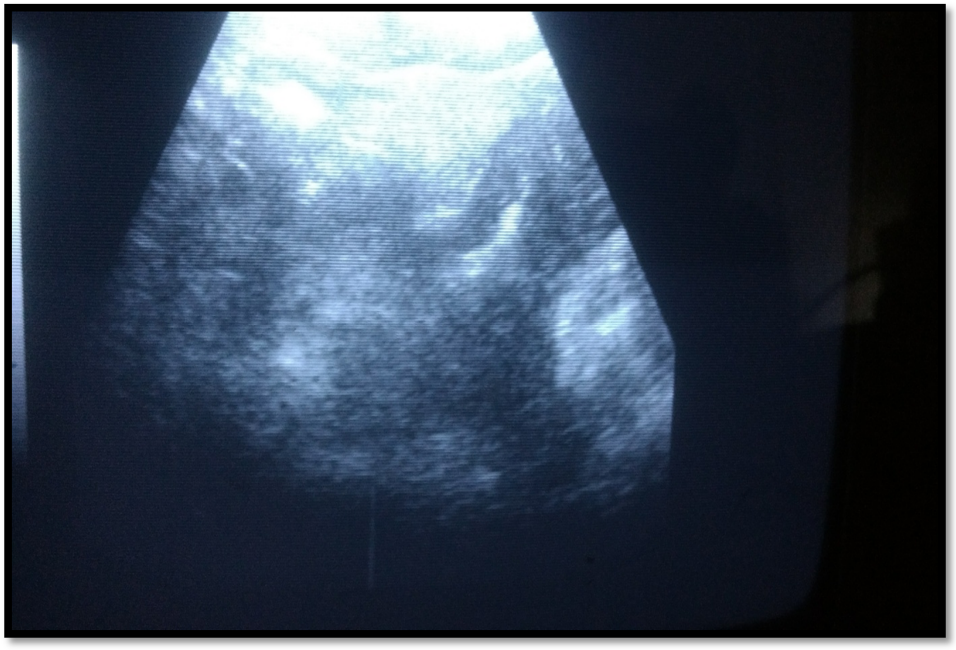


Plate 3: Ultra Sonogram showing uniform hyper echoic texture of pancreas

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VITA

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During her post-graduation, he has attended XIIIth Annual Convention of Indian Society for Advancement of Canine practise in April 2016 with 02research abstracts. Author has also published 3 research papers in reputed journals.

THESIS ABSTRACT

a)	Title of the thesis	:	**DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF DIABETES MELLITUS IN CANINE**
b)	Full name of student	:	**CHAUDHARI PRASHANT PRABHAKAR**
c)	Name and Address of Major Advisor	:	**DR. V. M. DHOOT** Assistant Professor, Department of Veterinary Clinical Medicine, Ethics & Jurisprudence, Nagpur Veterinary College, Nagpur.
d)	Degree to be awarded	:	**Master of Veterinary Science**
e)	Year of award of degree	:	**2017**
f)	Major Subject	:	**Veterinary Clinical Medicine, Ethics & Jurisprudence**
g)	Total number of pages in the thesis	:	**35**
h)	Number of words in the abstract	:	**341**
i)	Signature of Student	:	
j)	Signature, Name and address of forwarding authority	:	

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ABSRACT

The study entitled ‘ Diagnostic and therapeutic management of diabetes mellitus in canine” was carried out at the Teaching Veterinary Clinical Complex (TVCC)and Department of Veterinary Clinical Medicine, Ethics & Jurisprudence, Nagpur Veterinary College, Nagpur. The dogs presented at TVCC with symptoms

of polyuria, polydipsia, polyphagiaand obesity of 5 years and random blood glucose more than 150mg/dl were includedin the study.

Total 642 dogs showing typical symptoms of diabetes were screened. The data revealed the prevalence of 1.86 %. The highest occurrence was observed in Labrador (58.33 %), followed by Spitz (16.66 %) and 8.33 % each of Dachshund, Mongrel and Golden Retriever. Females were more affected as compare to males.

The common clinical symptoms included polyuria, polydipsia, polyphagia, obesity and lethargy. In one case, bilateral cataract was noticed whereas in four cases renal affections were noted.

Screened dogs were divided into two groups comprising of six animals in each group.Group I Dogs diabetes mellitus treated with a therapeutic regimen consistinga combination of Syrup Activated Zinc, Activated Arginine, Calcium Pantothanate L carnitine and lettuce extract @ 1 ml / 5 kg body weight.Group IIDogs diabetes mellitus were treated with recombinant insulin, @ 0.5 IU/kg, i/m, after meal at every 12 hrs interval**.** The haematobiochemical parameters indicated that the random and pre-prandial blood glucose levels did not differ significantly within the groups or between the groups. However, the dogs responded to recombinant insulin and post-prandial blood glucose levels significantly reduced in this group.

There was no significant effect on Serum Cholesterol, Serum Triglyceride, and BUN in any of the groups.

The haematological parameters such as TLC, Haemoglobin, PCV andTEC and biochemical parameter Serum Creatinine, did not show any significant difference within the days and between the groups. However, there was signifant differences in the values of neutrophil and lymphocyte counts in both the groups. The urinalysis indicated traces of glucose in all dogs and Ketonuria and proteinuria in 33.33 per cent cases, each. The urine samples revealed the presence *E. Coli* in 33% cases.

प्रबंध सारांश

अ.	प्रबंधाचे शिर्षक	:	''श्वानांतील मधूमेहाचे निदान व उपचार''
ब.	विद्यार्थ्याचे पुर्ण नांव	:	चौधरी प्रशांत प्रभाकर
क.	मार्गदर्शकाचे नांव व पत्ता	:	डॉ. व्ही. एम.धुत सहाय्यक प्राध्यापक पशुवैद्यकीय चिकित्सालयीन, नीती आणि न्यायवैद्यक शास्त्र विभाग, नागपूर पशुवैद्यक महाविद्यालय, नागपूर
ड.	प्रदान करण्यात येणारी पदवी	:	स्नातकोत्तर पदवी (एम.व्ही.एस.सी.)
इ.	पदवी प्रदान करण्याचे वर्ष	:	२०१७
फ.	मुख्य विषय	:	पशुवैद्यकीय चिकित्सालयीन, नीती आणि न्यायवैद्यक शास्त्र
ग.	प्रबंधातील एकूण पृष्ठे	:	३५
ह.	सारांशातील एकूण शब्द	:	२९८
ई.	विद्यार्थ्याची सही	:	
ज.	अग्रेषित करणाऱ्या अधिकाऱ्याची सही, नांव आणि पत्ता	:	(डॉ. एन. एन. झाडे) सहयोगी अधिष्ठाता नागपूर पशुवैद्यक महाविद्यालय, नागपूर

सारांश

'' श्वानांतील मधुमेहाचे निदान व उपचार या अध्यनांतर्गत पशुवैद्यकीय शैक्षणिक संकूल आणि पशुवैद्यकीय चिकित्सालयिन निती न्यायवैद्यक शास्त्र विभाग, नागपूर पशुवैद्यक महाविद्यालय, नागपूर येथे, मुत्र,तहान व भूक यांची वाढलेली मात्रा व स्थुलता इत्यादी लक्षणे असलेल्या ५ वर्षेव त्यावरिल श्वानांच्या रक्तातील साखरेची

१५० मि. ग्रॅ./ डे.ली. पेक्षा जास्त वाढलेली मात्रा इत्यांदीचा समावेश करण्यात आला.

मधुमेहाची लक्षणे असलेल्या एकुण ६४२ श्वानांची चाचणी करण्यात आली. त्यात एकंदरीत १.८६ टक्के मधूमेहाचा प्रभाव आढळून आला. त्यापैकी लॅब्राडोर जातींच्या श्वानात सर्वाधिक (५८.३३ टक्के) त्याखालोखाल स्पित्स (१६.३३) आणि डॅश्चहाऊंट,मोंगरेल व गोल्डन रेट्रीवर मध्ये अनुक्रमे १६.६६ टक्के व ८.३३ टक्के प्रभाव दिसून आला. तुलनात्मक दृष्टया मादी श्वानामध्ये नर श्वानापेक्षा जास्त प्रमाणात आढळले.

मुत्र,तहान, भूक इत्यादीच्या मात्रेत वाढ, स्थुलता आणि स्तुती इत्यादी लक्षणे असलेल्या श्वानांमध्येआढळून आले. तसेच एका वैद्यकीय प्रकरणात द्विपक्षीय मोतीबिंदु व ४ प्रकरणात मुत्रपिंड बाधीत झाल्याचे दिसून आले.

या अभ्यासांतर्गत मधुमेहग्रस्त श्वानांची दोन गटात विभागणी करण्यात आली एका गटात प्रत्येकी ६ श्वान गट–१ मधील मधुमेह ग्रस्त श्वानांवर सक्रिय झींक सिरप, सक्रिय आर्जिनीन, कॅल्सियम पेंटोथॅनेट–एल–कार्बिटीन आणि लेट्यूस अर्क १ मिली/५ किलो शरीराचे वजन, ने उपचार करण्यात आले, तर गट–२ मधील श्वानांवर पूर्नसंयोजित इन्शुलीन ०.५ आय यु/ किलो मात्रा जेवणानंतर प्रत्येकी १२ तासांच्या अंतराने उपचार करण्यात आले. रक्तजीवशास्त्रीय मापदंडाच्या आधारे एका गटात व दोन गटांतर्गत रक्ताच्या साखरेत, पूर्नसंयोजीत इन्शुलिनच्या उपचाराला प्रतिसाद दिलेल्या श्वानांमध्ये रक्तातील जेवणानंतरच्या साखरेची मात्रा परिणामकारक रित्या कमी झाली असल्याचे दिसून आले. रक्तद्रण्यातील युरिया नायट्रोजनवर कुठलाही परिणाम झाला नसल्याचे आढळून आले.

दोन्ही गटांवर करण्यात आलेल्या अभ्यासाच्या दिवसात रक्तगुणधर्माशास्त्रीय मापदंड जसे, टी एल सी हिमोग्लोबीन, पीसीव्ही आणि टीईसी, तसेच जीवरसायनशास्त्रीय मापदंड जसे, रक्तद्रव्यातील क्रेयाटिनीन मध्ये कुठलाही परिणामकारक फरक झाला नसल्याचे आढळून आले. तथापि,न्युट्रोफील आणि लिंफोसाईट या रक्तपेशीयांच्या संख्येत मात्र दोन्ही गटात परिणामकारक बदल झाला असल्याचे आढळून आले. मुत्र नमुन्यांच्या विश्लेषणातून सर्वच श्वानांच्या नमुन्यात कमी–अधिक प्रमाणात साखर व केटोन– युरिया व प्रोटिनयुरिया प्रत्येकी ३३.३३ असल्याचे आढळून आहे. मुत्राच्या ३३ टक्के नमुन्यात ई.कोलाय जीवाणू असल्याचे निर्दर्शात आले.