Kerbala Journal of Veterinary Medical Sciences Issue (2), Volume (1), (2025)

Diabetes Mellitus in Dogs and Cats: Etiology, Diagnosis and Treatment Approaches

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Received:9/7/2025 **Accepted**: 1/8/2025 **Published:** 15/9/2025

***Abstract* - Diabetes mellitus (DM) is a long-term illness that impacts both individuals and animals, particularly cats and dogs. Hyperglycemia and glycosuria are examples of clinical symptoms, and their persistence is documented for diagnosis. Important stages in the successful controlling diabetic mellitus include ensuring that the owners of cats or dogs are able to deliver insulin, identifying the clinical symptoms of deficiency control diabetes, and keeping an eye on blood sugar levels. Insulin resistance and obesity in dogs can be successfully handled by combining a varied diet also twice-daily insulin administration. The initial course of treatment for cats involves switching to a low-carb diet and receiving an insulin injection twice a day. In cats, remission can exceed 90%, however in dogs, the condition is typically lifelong unless a bias issue is secondary. The purpose of the study is to describe the pathophysiology, etiology, and feasible classification of impulsive diabetes mellitus in pets and emphasize cutting-edge studies carried out in this area**
***Keywords* - Diabetes mellitus, pet animals, cats, dogs**

INTRODUCTION

Diabetes mellitus (DM) is a long-term metabolic condition that arises when the body's defective insulin synthesis or response results in aberrant carbohydrate metabolism and elevated blood and urine glucose levels (1). DM it is the majority of notable and prevalent biochemical condition found in dogs and cats following people (2). It is difficult to diagnose and describe clinical symptoms in other large livestock, such as horses, buffalo, cattle, pigs, and other small ruminants. (3). The incapacity in beta cells to generate adequate insulin to meet the metabolic processes of the body needs is thought to be a key clinical sign of diabetes mellitus. Determining the development of diabetes mellitus depends on a number of criteria, including: (a) decreased synthesis of insulin, (b) decreased sensitivity to insulin of either organs or cells, and (c) increased production of other trustworthy hormones that cause DM (4,5). Hospitalization rates for diabetes in dogs and cats ranged from 0.4% to 1.2% (6). Polydipsia, polyuria, and weight loss are common medical signs of diabetes. Only when hyperglycemia above the renal threshold of amounts that cause glycosuria—220–270 mg/dL in cats and 180–220 mg/dL in dogs, respectively—do these noteworthy clinical signs (7).

Classification :

Although it has species-specific traits, diabetes mellitus in pets, especially dogs and cats, can be categorized similarly to diabetes in humans (7). An outline of the classification can be found here.

Classification of Diabetes Mellitus in Pet Animals:
1. Type I Diabetes Mellitus (Insulin-Dependent):
* produced by immune-mediated death of pancreatic β-cells;
* more prevalent in dogs
*causes a complete lack of insulin (8).
*Usually necessitates ongoing insulin treatment.
Common Causes:
* genetic propensity (for instance, in breeds such as Poodles, Miniature Schnauzers, and Samoyeds).
* Pancreatitis.
* Autoimmune conditions.

2. Type II Diabetes Mellitus (Non-Insulin-Dependent):
*Insulin resistance and relative insulin insufficiency are characteristics.
* more prevalent in cats.
*Diet, weight control, and oral hypoglycemic medications may be effective in the early stages.

*It could lead to insulin dependence.

Factors that Participate:
* being overweight.
* A lack of physical exercise.
* Concurrent conditions (such as hyperadrenocorticism and acromegaly).
*pancreatic islet amyloidosis (frequent in cats).

3. Secondary Diabetes Mellitus:
* Occurs as a consequence of another illness or drug.
*observed in both cats and dogs.
Causes:
*Endocrine disorders: hyperthyroidism, acromegaly, and Cushing's disease in dogs and cats, respectively.
* Extended usage of drugs, such as progestagens and glucocorticoids.
* Pancreatic neoplasia or pancreatitis**.**

4. Gestational Diabetes (Rare in Pets) :
*Sometimes observed in intact female canines.
* this condition is caused by hormonal changes during pregnancy that result in insulin resistance**.**
***It usually goes away following parturition or spaying.**

Table 1. show types and causes of DM .

Type	**Species affected**	**Cause**	**Insulin dependence**
Type I	Dogs(mainly)	Immune-mediated β-cell destruction	Yes (lifelong)
Type II	Cats(mainly)	Insulin resistance ± β-cell loss	Often not initially, may become dependen
Secondary Diabetes	Both	Other diseases/drugs	Depends on underlying ca
Gestational Diabetes	Dogs(rare)	Hormonal (pregnancy)	Temporary

Etiology

The collapse of the pancreatic beta cells, which is a normal consequence of autoimmune activity, is a characteristic of type 1 diabetes. Complete beta cell death results in reduced insulin production (9) .

There is no doubt that canine type 1 diabetes has a complex etiology. Family ties, Keeshond's genealogy study, and genomic studies that focused on identifying haplotypes of the defensive and perceptive major histocompatibility complex have all been used to suggest genetic predisposition (10). Numerous genes linked to human sensitivity to diabetes were also linked to increased risk of diabetes in dogs. The same haplotypes and genotypes that are present in the majority of susceptible Species are also present in dogs with diabetes that have a class II major histocompatibility complex gene. Furthermore, several dogs have been found to have components that mediate immunity of diabetes development (10,11). Over the past decade, researchers have concentrated on canine etiological variables, such as autoantibodies, relevant genetic material, dog leukocyte antigen (DLA), which promotes diabetes mellitus, and their interactions (1,12). The compatible incident with pubertal disease was confirmed to be an uncommon occurrence by studies conducted on dogs younger than 12 months (13,14,15). Furthermore, around 70% of verified instances involving female dogs suggested that they would be extremely vulnerable to DM (16). On the other hand, other research confirms that the incidence of DM in men and women may be equal (17).

Canine DM identification in general Dogs as young as 4 to 18 years old can receive DM with good results, whereas the age range of 7 to 9 is the natural average (18). For the most part, all dog breeds exhibit the same degradation of Langerhans isolates. About half of dogs with new diagnoses thought that auto-antibodies might be the cause of beta cell loss (19). Cats rarely develop DM-type 1 compared to dogs. It was just reported that some cats have lymphocytic pervasive insulitis, which is believed to be a sign of an illness mediated by the immunological system (20). With the exception of specific characteristics like obesity, midsize, and age, as well as low blood insulin levels or amyloid accumulation in the Langerhans islets with beta cell destroying, finally, retinal and complexes, diabetes mellitus in cats shares the same clinical and pathophysiological characteristics as type-2 diabetes in humans (21). During the initial phase of diabetes mellitus (DM), insulin production declines in response to glucose., and in the second stage, the response is skewed (22). Amyloid of Langerhans islets, lipid toxicity, and glucotoxicity are all strongly linked to the onset and development of diabetes mellitus, particularly NIDDM type-2 in cats. These cat confirmational models demonstrated the impact of glucose on the Langerhans islets after ongoing intraperitoneal glucose administration to create a vacuole at the Langerhans cell, which will lead to diabetes mellitus. Targeting insulin tissue and causing damage to the structure and function of beta cells may be crucial objectives of hyperglycemia treatment in order to preserve beta cells and ameliorate DM (23). However, via phosphorylating pancreatic and duodenal homeobox 1 (PDX1), glucose stimulates the manufacture of insulin by stimulating the transcription gene of insulin (22, 23).

Along with elements like physical inertia, sex (females are less risky than males), confinement, aging, and the use of progestin and glucocorticoids, obesity is the most harmful event for the advancement of diabetes

mellitus in felines. A drop in insulin perceptivity of more than 50% was associated with a median gain of about 1.9 kg by consumption studies. According to an experimental investigations conducted on cats. Individual differences exist in insulin sensitivity, and it is hypothesized that cats with intrinsically poor insulin sensitivity are more likely to acquire resistance after increasing weight (24). The first adipose-derived factor thought to explain the connection between insulin resistance and obesity observed in people with type 2 diabetes was tumor necrosis factor (TNF). Insulin signaling is aggressively negatively impacted by TNF. Another factor that negatively affects beta cell function and Hyperglycemia in cats is a condition known as glucotoxicity, while lipotoxicity refers to the detrimental effects of increased quantities of free fatty acids in the bloodstream on beta cell activity [25,26].

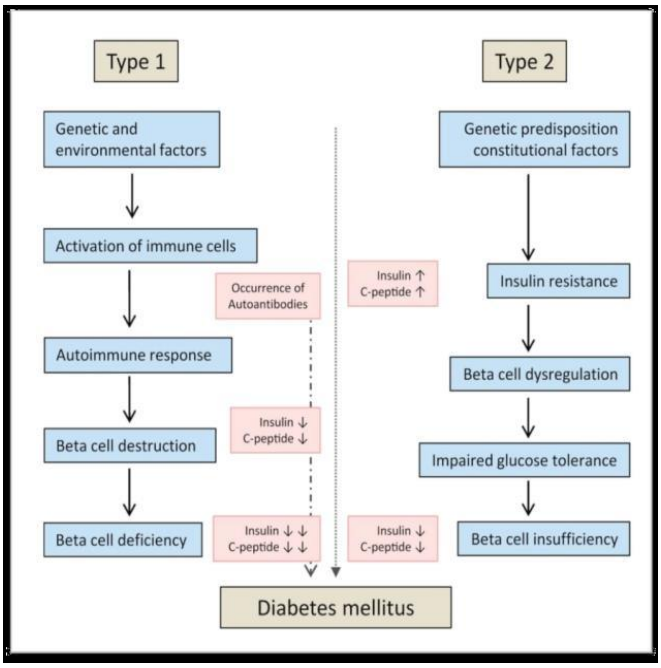

Figure 1. Pathological occurrences that result in type 1 DM and type 2 DM (27) .

Pathophysiology:

The pathophysiology of diabetes mellitus (DM) in pets usually includes a number of variables, This includes as resistance to insulin, insulin insufficiency, and maybe other underlying disorders. Pancreatic amyloidosis in cats or immune-mediated loss of beta cells (the insulin-producing cells in the pancreas) in dogs can both cause insulin insufficiency (27, 28). Another important factor, especially in cats, is insulin resistance, which occurs when the body's cells don't react to insulin as they should. Additionally, both dogs and cats may develop diabetes as a result of environmental variables such obesity and genetic predisposition (29).

- **Insulin Deficiency:**

Dog diabetes often resembles human type 1 diabetes, in which the immune system attacks and destroys the beta cells in the pancreas (30). As a result, Blood sugar levels rise as a result of inadequate insulin, which prevents glucose from entering cells.Insulin production may be hampered in cats with pancreatic amyloidosis, a condition in which deposits resembling starch build up in the pancreas.

- **Insulin Resistance:**

In cats, insulin resistance is a major contributor to diabetes, often associated with obesity.Cats that are obese exhibit altered insulin signaling and hyperglycemia transporter genes, making their cells less responsive to insulin(31).

- **Other Factors:**

a. hereditary Predisposition: There may be a hereditary component to diabetes, as some dog and cat breeds are more likely to develop it (32).

b. Environmental variables: Diabetes and insulin resistance may be exacerbated by obesity, a high-fat diet, and other environmental variables (33).

c. Exocrine Pancreatic Disease: Diabetes in dogs can result from pancreatitis, or inflammation of the pancreas, which damages the exocrine and endocrine components of the organ (34).

d. Additional Medical Conditions: Diabetes can be exacerbated by insulin resistance brought on by conditions such as hyperadrenocorticism (Cushing's disease) in dogs (35).

Pathophysiology of Hyperglycemia:

Glucose cannot enter cells for energy when insulin is insufficient or cells are resistant to its actions. This results in hyperglycemia, or elevated blood sugar, which can harm the kidneys, eyes, and nerves, among other organs (36).

Diagnosis :

Diabetes diagnosis requires the presence of appropriate clinical indicators, as well as persistent glycosuria and hyperglycemia. Nonetheless, hypertriglyceridemia and hypercholesterolemia are both prevalent, whereas ketoacidosis and ketonuria can develop when the owner is unable to recognize early symptoms or is slow to seek veterinary care (37). Cats and dogs with clinical signs of diabetes mellitus may undergo physical examinations, as well as complete laboratory tests that can be used to diagnose and rule out other illnesses, such as triglycerides (TG), thyroxine (T4), blood pressure (BP), urine culture with analysis, urine protein: creatinine ratio (UPC), and complete blood count (CBC) (38). When blood glucose levels rise above 250–300 mg/dL in cats and 200 mg/dL in dogs, progressive glucosuria typically occurs (39).As long as

there is ongoing glycosuria and hyperglycemia, clinical signs of diabetes will manifest (40). When blood sugar levels fall Among the high citation concentrations and levels of the renal threshold, these symptoms do not appear. Both Dogs and cats appear healthy, keep up a consistent mass, are just detectable through normal lab testing in the early stages of non-clinical DM (41). In addition to the aforementioned, some people may exhibit weakness, asthenia, and inactivity. The following are the fundamental estimation criteria for diabetic cats and dogs (39,41) :

•assess the animal's general health (a thorough physical examination and dietary and concurrent medication history are checked).

•identifying any issues that might be connected to the illness, such as canine cataracts and feline peripheral neuropathy.

• identifying any coexisting issues that are typically connected to the illness (e.g. pancreatitis and infection of the urinary tract).

• Identifying situations that could affect how well a patient responds to treatment, such as hyperthyroidism, hyperadrenocorticism, and kidney illness.

•calculating the danger signs for female dogs, e.g. obesity, die estrus, insulin resistance, and pancreatitis.

In addition to increased triglycerides and cholesterol, glucosuria, hyperglycemia, and stress leukograms are frequently found. Dogs consistently show elevated levels of alanine aminotransferase (ALT) and alkaline phosphatase (ALP), whereas cats exhibit higher levels of ALP and greater variability in the stress leukogram (42).increased liver enzyme levels in cats may support additional liver disease evaluation (43). One common concurrent condition that may need treatment is pancreatitis. Because of osmotic diuresis, dehydration, metabolic acidosis, and coma , diabetic dogs and cats with ketoacidosis may experience severe spikes in blood glucose levels, azotemia, and a decrease in total minor carbon dioxide (CO2) (44). Urine analysis without casts will reveal the presence of glucose or protein ketones on bacteria (45). Because infection is frequent in animals with glucosurine, a urine culture should be used (46).

Treatment :

Insulin therapy and dietary changes are the main treatments for diabetic mellitus (DM) in dogs and cats. Insulin is used to control blood glucose levels; it is usually injected subcutaneously. Dietary adjustments are also essential for diabetic management, with an emphasis on regular meal scheduling and food selection.

1-Insulin Therapy:

- **Type of Insulin:**

Depending on the specific requirements of the pet, veterinarians may suggest various forms of insulin, such as lente for dogs or Insulins with a long half-life (Protamine Zinc Insulin [PZI] or gargine)for cats.

- **Dosage and Frequency:**

A veterinarian determines the appropriate insulin dosage and frequency of injections, which can change depending on the pet's weight, blood sugar levels, and general health.

- **Twice-Daily Injections:**

For stable blood glucose levels, many diabetic pets need twice-daily insulin injections, frequently prior to meals.

2- Dietary Modification:

• **Regular Meal Schedule:** Pets with diabetes should be fed at regular intervals, with meals being consumed right before or right before insulin is administered.

• **A well-rounded diet:** Blood glucose levels can be controlled with a diet rich in protein and low in carbs.

• **Weight Management:** Controlling diabetes and avoiding complications require maintaining a healthy weight.

• **Veterinary Advice:** When it comes to the kind and quantity of food that a pet with diabetes should be fed, veterinarians can offer precise advice.

Additional Things to Think About:

• **Frequent Monitoring:** Diabetes management for pets requires regular veterinary examinations, blood and urine testing, and tracking of the pet's weight, appetite, drinking, and urination.

• **Exercise:** Depending on the pet's age, weight, and general health, regular exercise can help regulate blood sugar levels and enhance insulin sensitivity.

• **Early Detection and Treatment:** Preventing problems and enhancing the quality of life for pets with diabetes can be achieved through early diagnosis and treatment.

• **Lifetime Commitment**: Consistent therapy, close observation, and dietary modifications are necessary for the lifetime management of diabetes in pets.

In actuality, the treatment options is similar as those used for diabetes in humans, and they include injections of insulin twice daily with 12-hour intervals, dietary changes, obesity correction, oral hypoglycemic medications for cats, and exercise for dogs. Dogs and cats have diverse therapeutic approaches, in part because of their different underlying etiologies. In general, the pattern utilized in human medicine may not be the same for the classification of (DM)in feline and canine (11).

Cats with blood sugar can be managed with minimal symptoms, such as no clinical signs, a healthy lifestyle, and acceptable medication responses. Adverse complications of the disease, such as peripheral neuropathy, diabetic ketoacidosis, and hypoglycemia, can also be delayed or develop. Achieving excellent

glucose level control within 6 months of diagnosis with careful home monitoring, stopping against insulin medications, and using Detemir of insulin (Lantus) or glargine (Levemir)in conjunction with a decrease -carb food are all indicators of diabetic absolution in cats. The most effective way to treat Cats with diabetes is to begin Insulin treatment with Protamine zinc insulin (PZI; Prozinc) or glargine (Lantus) at a starting dose of 1-2 U/ kg every 12 hours (47, 48).Insulin treatment is typically required to treat clinical diabetes mellitus in dogs. According to the Task Force, the best option for treating dogs is Vetsulin (porcine insulin zinc suspension) with U-40 pork lente which should be started at a every 12 hours at a dose of 0.25 U/kg (43).For many dogs, the activity period is close to 12 hours, and formless insulin components help to lower postprandial hyperglycemia. A medically unwell and Keto dog must respond to twenty four-hour care for progrese therapies in ketosis and other basic ailments, just like diabetic cats do. Delaying suggestive hypoglycemia, which can happen when the insulin dosage is significantly increased, is a crucial goal of treatment (44).

Therapy complications :

Both the direct consequences of inadequate blood sugar control and the indirect consequences of disease management can constitute therapy problems in diabetic pets, particularly dogs. Low blood sugar, or hypoglycemia, is a frequent side effect that can be harmful if left untreated. Diabetic neuropathy, cataracts, urinary tract infections, and diabetic ketoacidosis (DKA) are further consequences. Pets with diabetes, particularly dogs, may experience severe therapy problems that need to be carefully managed. Common consequences include hypoglycemia, diabetic ketoacidosis, cataracts, UTIs, and diabetic neuropathy. For diabetic pets, minimizing complications and enhancing their quality of life requires proper insulin, food, exercise, and home monitoring management. Both the owner and the veterinarian may find it difficult and irritating if the clinical signs persist or are frequent (45). Insulin activity is typically caused by worries about insulin's bioactivity, storage, or responsiveness. When hyperglycemia was controlled with doses greater than 1.5 to 2.0 IU/kg per injection, insulin resistance should be suspected (46). Depending on further clinical symptoms or pathophysiological characteristics, the appropriate examinations should be used. A common side effect of insulin therapy is hypoglycemia, which can be brought on by an unanticipatedly high increase in insulin dosage, an excessive insulin dosage, periods of inactivity, or strenuous activities (47Hypoglycemia can cause coma, paroxysm, ataxia, asthenia, and lethargy. Increases in glycogenolysis, glucagon, growth hormone, glucocorticoids, and adrenaline are causes of this pathological reaction to hypoglycemia. All of the aforementioned cause a noticeable rise in blood sugar levels within 12 hours, which lasts for two to three days and is accompanied by the symptoms of hyperglycemia. If the dogs continue to exhibit the usual clinical indications of diabetes mellitus, it is assumed that their condition is out of control and that they need a higher dosage of insulin. Sequential blood glucose testing and hospitalization are required for the detection of the Somogyi phenomenon (reaction). The dosage reduction is guaranteed when the Somogyi effect manifests (46). Excessive disruption of insulin duration may increase the risk of hypoglycemia. It is frequently observed ten hours or more after the injection when the glucose reaches its lowest levels. Treatment options include reducing the frequency of injection or switching to an insulin type that acts more quickly. It can be challenging and stressful to manage diabetes in pets, but all diabetic pets can have their diabetes under control with the right owner education, observation, and understanding of the variables that can be controlled (44,49).

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