Review Article

# CANINE DIABETES MELLITUS: A COMPREHENSIVE REVIEW OF PATHOGENESIS, DIAGNOSIS, AND MANAGEMENT STRATEGIES

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## ABSTRACT

*Canine diabetes mellitus is a common endocrine disorder in dogs, closely resembling type 1 diabetes in humans, and is marked by chronic hyperglycemia from pancreatic β-cell destruction or dysfunction, causing insulin deficiency. Contributing factors include genetic predisposition, hormonal imbalances, pancreatitis, and certain drugs. It occurs most often in older, female, and breed-susceptible dogs. Typical signs include polyuria, polydipsia, weight loss, and bilateral cataracts, with diagnosis based on persistent fasting hyperglycemia and glucosuria. Management requires lifelong insulin therapy, dietary control, and monitoring through tools such as blood glucose curves and Fructosamine testing. Complications like diabetic ketoacidosis, cataracts, and urinary tract infections are frequent and need timely intervention. Advances in continuous glucose monitoring, immunotherapy, and molecular diagnostics have improved outcomes. With proper therapy and owner compliance, affected dogs can maintain a good quality of life. Research is focusing on early detection, genetic screening, and innovative treatments like stem cell therapy and pancreatic islet regeneration, ensuring continued progress in controlling this complex disease.*

**Keywords:** pancreatitis, hyperglycemia, dietary control, insulin deficiency, insulin therapy

Received :10.08.2025 Revised : 28.08.2025 Accepted : 04.09.2025

## INTRODUCTION

Canine diabetes mellitus (DM) is a common endocrine disorder characterized by persistent hyperglycemia due to either an absolute or relative deficiency of insulin secretion or action (Catchpole *et al.,* 2005). The disease shares many features with human diabetes but also displays unique clinical patterns and aetiologies specific to dogs (Nelson and Reusch, 2014). It represents a significant cause of morbidity and requires lifelong management, often imposing emotional and financial burdens on pet owners (Mattin *et al.*, 2014).

The prevalence of DM in dogs has been reported to range between 0.2% and 1.3%,

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depending on the population and geographic location studied (Fall *et al.*, 2007). In recent decades, the incidence appears to be increasing, potentially due to heightened awareness, improved diagnostics, and increasing obesity trends among pet populations (Davison *et al.,* 2005; Catchpole *et al*., 2008). Female dogs and neutered animals are more frequently affected, and certain breeds such as Samoyeds, Miniature Schnauzers, and Poodles show a higher predisposition (Guptill *et al*., 2003; Mattin *et al.*, 2014).

Unlike in cats and humans, where Type 2 diabetes mellitus predominates, most dogs suffer from insulin-dependent or Type 1 diabetes mellitus, characterized by complete destruction of pancreatic beta cells (Rand *et al.,* 2004). This form necessitates exogenous insulin therapy from the time of diagnosis (Nelson, 2015). Contributing factors include genetic susceptibility, autoimmune destruction of beta cells, pancreatitis, hormonal disorders, and certain drug therapies (Catchpole *et al.,* 2008; Hess *et al.,* 2000). Diagnosis typically occurs when clinical signs—such as polyuria, polydipsia, polyphagia, and weight loss; are evident, often accompanied by marked hyperglycemia and glucosuria (Fleeman and Rand, 2001). However, earlier detection remains a clinical challenge, especially in cases with concurrent diseases that mask or alter the typical presentation (Reusch, 2002).

Effective management requires a multifactorial approach, including insulin therapy, dietary regulation, monitoring, owner education, and regular veterinary oversight (Fleeman and Rand, 2001; Nelson and Reusch, 2014). Despite these advances, diabetic dogs remain susceptible to complications such as cataracts, urinary tract infections, and diabetic ketoacidosis (Keenan *et al.*, 2003).Emerging areas of research focus on refining insulin delivery, enhancing monitoring through technology such as continuous glucose monitoring systems (CGMS), and exploring the role of genetics and immunology in the disease's pathogenesis (Zini *et al.*, 2010; Gilor *et al.,* 2016). The future of canine diabetes management lies in improving owner compliance, minimizing complications, and possibly one day achieving beta-cell regeneration or immunotherapy (Fleeman and Rand*,* 2013).

This review will discuss the epidemiology, pathogenesis, clinical features, diagnostic techniques, management options, complications, and future directions in canine diabetes mellitus, with emphasis on evidence-based findings and emerging innovations.

## EPIDEMIOLOGY

### Prevalence and Incidence

The reported prevalence of canine diabetes mellitus (DM) varies geographically, with estimates ranging between 0.2% and 1.3% across different studies and populations (Davison *et al.*, 2005; Fall *et al*., 2007). In the United Kingdom, a large-scale study involving over 200,000 dogs estimated an overall prevalence of 0.34%, with marked breed differences (Mattin *et al*.,

2014). In Sweden, data from an insured dog population revealed an incidence of 13.1 per 10,000 dog-years at risk, highlighting the disease's importance in clinical practice (Fall *et al.,* 2007).

The incidence of canine diabetes appears to be increasing over time, potentially due to improved diagnostics, better awareness among veterinarians and pet owners, and rising obesity rates (Catchpole *et al.*, 2005; Guptill *et al.*, 2003). Furthermore, advances in medical care have enhanced survival of dogs with predisposing conditions such as pancreatitis and hyperadrenocorticism, which may indirectly raise diabetes prevalence (Hess *et al.*, 2000).

**Breed Predisposition**

Certain breeds demonstrate a higher risk of developing diabetes, suggesting a strong genetic component (Catchpole *et al.,* 2008). Breeds with consistently elevated risk include Samoyeds, Miniature Schnauzers, Miniature Poodles, Cairn Terriers, and Dachshunds (Mattin *et al.,* 2014; Fall *et al*., 2007). In contrast, some breeds such as Boxers and German Shepherds are rarely affected, indicating possible protective genetic factors (Davison *et al.*, 2005; Guptill *et al*., 2003).

Genetic investigations have revealed that insulin gene polymorphisms and immune-mediated beta-cell destruction may be involved in the breed-specific predisposition (Catchpole *et al*.,2008b; Sidhu *et al.*, 2019). In particular, the presence of certain dog leukocyte antigen (DLA) haplotypes has been associated with increased risk in breeds such as the Samoyed and Tibetan Terrier (Short *et al*., 2007).

**Age and Sex Distribution**

Canine diabetes typically occurs in middle-aged to older dogs, with most cases diagnosed between 7 and 10 years of age (Guptill *et al.,* 2003; Mattin *et al.,* 2014). Juvenile-onset diabetes is rare but has been reported in breeds like Golden Retrievers and Keeshonds, often with a suspected hereditary component (Nelson, 2015; Catchpole *et al.,* 2008a).

Sex also influences disease distribution. Intact females were historically considered more prone, particularly during dioestrus due to progesterone-mediated insulin resistance (Rand *et al.*, 2004). However, in many modern studies, neutered males now outnumber females, possibly reflecting changing demographics in pet populations (Mattin *et al.*, 2014; Davison *et al*., 2005).

**Risk Factors and Environmental Influences**

Several risk factors contribute to the development of diabetes in dogs. Obesity is increasingly recognized as a modifiable risk factor, as adipose tissue promotes systemic inflammation and insulin resistance (Mattin *et al.,* 2014; Hoenig, 2002). Chronic pancreatitis is another critical factor, with the destruction of exocrine and endocrine tissue leading to irreversible insulin deficiency (Hess *et al.,* 2000).

Endocrine disorders such as hyperadrenocorticism and hypothyroidism may promote hyperglycemia and insulin resistance, thereby increasing diabetes risk (Gilor *et al.,* 2016). Furthermore, the administration of diabetogenic drugs like glucocorticoids and progestins has been implicated in the pathogenesis of secondary diabetes (Fleeman and Rand, 2001).

## CLASSIFICATION AND TYPES OF CANINE DIABETES MELLITUS

### Insulin-Dependent Diabetes Mellitus (IDDM – Type 1)

The most common form of diabetes mellitus in dogs is insulin-dependent diabetes mellitus (IDDM), often equivalent to Type 1 diabetes in humans (Catchpole *et al.*, 2005). It is characterized by an absolute deficiency of insulin due to immune-mediated destruction or degeneration of pancreatic beta cells (Nelson and Couto, 2014). Most diabetic dogs are permanently insulin-dependent from the time of diagnosis (Fleeman and Rand, 2001).

Autoimmune mechanisms have been proposed in the pathogenesis of IDDM, with histological evidence of lymphocytic infiltration (insulitis) observed in a subset of dogs (Davison *et al.*, 2003). Additionally, insulin autoantibodies and specific DLA class II haplotypes have been implicated in genetic susceptibility (Catchpole *et al.*, 2008a; Short *et al.*, 2007).

### Non-Insulin-Dependent Diabetes Mellitus (NIDDM – Type 2-like)

Although rare, some dogs may exhibit features of non-insulin-dependent diabetes mellitus (NIDDM), resembling Type 2 diabetes in humans (Rand *et al.*, 2004). This form is marked by insulin resistance and varying degrees of beta-cell dysfunction but not complete destruction (Gilor *et al.,* 2016). It is often associated with obesity, hyperadrenocorticism, or dioestrus, where hormonal imbalances promote insulin resistance (Hoenig, 2002).

Unlike in cats, true remission is exceedingly rare in dogs, and even dogs with initial insulin resistance often progress to complete insulin dependence (Nelson, 2015).

### Secondary Diabetes Mellitus

Secondary diabetes arises from identifiable underlying conditions or drugs that interfere with insulin action or secretion (Hess *et al*., 2000). Common causes include hyperadrenocorticism, chronic pancreatitis, hypersomatotropism, and use of diabetogenic medications like glucocorticoids and progestins (Fleeman and Rand, 2001; Gilor *et al*., 2016).

In these cases, resolution of the primary disease may not always reverse diabetes, particularly if permanent beta-cell damage has occurred (Hess *et al.,* 2003). Therefore, these dogs typically require ongoing insulin therapy even after treating the initiating factor (Nelson, 2015).

### Transient and Gestational Diabetes

Transient diabetes is rarely observed in dogs and generally occurs during dioestrus or gestation due to progesterone and growth hormone–mediated insulin resistance (Rand *et al.,* 2004). If detected early and the inducing hormonal influence is removed (e.g., via ovariohysterectomy), the diabetic state may resolve without long-term therapy (Nelson, 2015).

Gestational diabetes is exceptionally rare but may develop in intact females due to hormonal changes associated with pregnancy (Davison *et al.*, 2003). Early detection and prompt intervention are crucial for maternal and foetal health.

### Juvenile-Onset Diabetes

Juvenile diabetes, though uncommon, has been reported in certain breeds such as Golden Retrievers and Keeshonds, often with a suspected autosomal recessive inheritance pattern (Catchpole *et al.*, 2008b). Affected dogs usually require insulin therapy from a very young age, and the disease resembles human Type 1 diabetes in its pathogenesis (Davison *et al.*, 2003).

## PATHOPHYSIOLOGY OF CANINE DIABETES MELLITUS

### Destruction or Dysfunction of Pancreatic Beta Cells

The hallmark of canine diabetes mellitus is the loss or functional impairment of insulin-producing beta cells in the islets of Langerhans (Nelson and Reusch, 2014). In many cases, this occurs due to chronic immune-mediated insulitis or idiopathic degeneration, resulting in absolute insulin deficiency (Davison *et al*., 2003). Histopathological studies often reveal islet atrophy, fibrosis, or lymphocytic infiltration (Catchpole *et al.,* 2005).In the liver and skeletal muscles, glucose is stored as glycogen and in adipocytes it is stored as triglycerides (Sidhu *et al.,* 2019).

Beta-cell destruction leads to reduced glucose uptake by insulin-sensitive tissues like muscle and adipose, and increased hepatic glucose production, contributing to persistent hyperglycemia (Rand *et al.,* 2004).

### Insulin Resistance

Insulin resistance can precede or exacerbate diabetic states in dogs, particularly in females during dioestrus or those with underlying endocrinopathies such as hyperadrenocorticism (Fleeman and Rand, 2001). In these scenarios, excess hormones (e.g., progesterone, cortisol, growth hormone) antagonize insulin action at the receptor and post-receptor levels (Hoenig, 2002).

This pathophysiological mechanism plays a critical role in secondary and transient diabetes, often overlapping with primary beta-cell failure (Gilor *et al.*, 2016).

### Hepatic Gluconeogenesis and Glycogenolysis

In the absence of insulin, hepatic gluconeogenesis and glycogenolysis are unopposed, contributing significantly to hyperglycemia (Nelson, 2015). Insulin normally inhibits glucose production in the liver, but its deficiency leads to increased expression of gluconeogenic enzymes and mobilization of substrates like amino acids and lactate (Gilor *et al.*, 2016).

Furthermore, the liver's failure to store glucose as glycogen results in an energy-deficient state despite systemic hyperglycemia (Rand *et al*., 2004).

### Lipid Metabolism Alterations

Insulin also plays a vital role in lipid metabolism, and its deficiency causes enhanced lipolysis, leading to elevated levels of free fatty acids (Hoenig, 2002). These substrates are diverted to the liver for ketogenesis, which in poorly controlled cases leads to diabetic ketoacidosis (DKA) -a life-threatening complication (Fleeman and Rand, 2001).

Hyperlipidaemia and hepatic lipidosis are common in canine diabetics due to chronic mobilization of fats and impaired lipid clearance (Catchpole *et al*., 2005).

### Protein Catabolism

Lack of insulin also results in accelerated proteolysis, primarily in skeletal muscle, contributing to weight loss and muscle wasting (Gilor *et al.*, 2016). This increased protein turnover provides gluconeogenic substrates, further worsening hyperglycemia (Nelson and Couto, 2014).

## CLINICAL SIGNS AND DIAGNOSIS

### Classical Clinical Signs

The most commonly reported clinical signs in canine diabetes mellitus are polyuria, polydipsia, polyphagia, and weight loss despite a good appetite (Nelson and Couto, 2014). These manifestations are primarily due to persistent hyperglycemia exceeding the renal threshold (~180 mg/dL in dogs), leading to glucosuria and osmotic diuresis (Gilor *et al.,* 2016). Increased water intake compensates for the fluid loss through urination, while weight loss results from lipolysis and proteolysis due to insulin deficiency (Fleeman and Rand*,* 2001).

Owners also frequently report lethargy, reduced activity, and poor hair coat, especially in longstanding or poorly managed cases (Catchpole *et al.,* 2005).

### Dermatological and Ophthalmological Manifestations

Alopecia, thin skin, and secondary pyoderma are often seen due to immunosuppression associated with chronic hyperglycemia (Hoenig, 2002). Cataract formation is considered pathognomonic in diabetic dogs, occurring in over 75% of affected animals within a year of diagnosis (Beam *et al.*, 1999). The lens accumulates sorbitol due to high glucose levels via the

aldose reductase pathway, leading to osmotic damage and lens fiber swelling (Williams *et al.,* 2006).

Sudden onset of bilateral cataracts is often the first clinical sign prompting veterinary consultation (Davidson, 2003).

**Signs of Complicated Diabetes**

Dogs with diabetic ketoacidosis (DKA) show more severe signs such as vomiting, dehydration, acetone breath, weakness, and even coma (Nelson, 2015). Inappetence and mental dullness may be the only initial clues, and without rapid intervention, DKA can be fatal (Gilor *et al.*, 2016). Concurrent infections such as urinary tract infections may exacerbate clinical signs and complicate glycaemic control (Fleeman and Rand*,* 2001).

**Differential Diagnoses**

Several disorders can mimic or coexist with diabetes mellitus. These include hyperadrenocorticism, renal glycosuria, chronic renal failure, and liver diseases (Rand *et al.,* 2004). Accurate diagnosis requires ruling out these conditions using appropriate diagnostics such as ACTH stimulation tests, bile acids, and urinalysis. Transient diabetes due to estrus-induced insulin resistance or pancreatitis should also be differentiated (Catchpole *et al.,* 2005). Systemic hypertension has also been reported in dogs suffering from Diabetes Mellitus (Kour *et al* 2020).

**Diagnostic Criteria and Initial Workup**

Diagnosis is confirmed by persistent fasting hyperglycemia (>200 mg/dL) and glucosuria on at least two separate occasions, in a dog with compatible clinical signs (Nelson and Couto*,* 2014). Fructosamine levels are often used to confirm chronic hyperglycemia (>350 µmol/L) and distinguish true diabetes from stress-induced hyperglycemia (Gilor *et al*., 2016). Additional tests include complete blood count, serum biochemistry, and urinalysis to identify concurrent illnesses.Baseline diagnostics also help guide therapeutic choices and prognosis (Fleeman and Rand, 2001).

**DIAGNOSTIC TESTING AND MONITORING**

**Blood Glucose Monitoring**

Measurement of fasting blood glucose is a fundamental tool in both diagnosis and ongoing monitoring of diabetic dogs (Nelson and Couto, 2014). Repeated hyperglycemia >200 mg/dL, particularly alongside glucosuria and compatible clinical signs, confirms diabetes mellitus (Gilor *et al.*, 2016). Spot checks may be unreliable due to stress hyperglycemia, so serial glucose curves are preferred (Fleeman and Rand, 2001).Glucose curves involve measuring blood glucose every 1–2 hours over a 12–24-hour period to assess insulin efficacy and nadir levels (Rand *et al.*, 2004).

**Fructosamine and Glycated Haemoglobin**

Fructosamine reflects the average blood glucose concentration over the previous 1–3 weeks and is less affected by acute stress (Feldhahn *et al.*, 1999). A value >350 µmol/L typically supports a diagnosis of diabetes (Strage *et al.,* 2002). Glycated haemoglobin (HbA1c) provides an even longer-term view (8–12 weeks), though it is less commonly used in veterinary practice (Hoenig, 2002).Fructosamine is especially useful in animals with white-coat syndrome or stress-induced hyperglycemia (Nelson, 2015).

**Urinalysis and Urine Culture**

Urinalysis often reveals glucosuria and proteinuria, and may also identify ketonuria in dogs with diabetic ketoacidosis (Gilor *et al.,* 2016). Since diabetic dogs are prone to urinary tract infections (even subclinical), a urine culture is recommended at diagnosis and periodically thereafter (Fleeman and Rand*,* 2001).Pyuria and bacteriuria may not always be present, so culture is essential even in asymptomatic cases (Catchpole *et al*., 2005).

**Serum Biochemistry and CBC**

A comprehensive metabolic profile aids in detecting concurrent diseases (e.g., pancreatitis, hepatic lipidosis, renal disease) and helps assess glucose, cholesterol, triglycerides, liver enzymes, BUN, and creatinine (Rand *et al.*, 2004). A CBC may reveal neutrophilia, anemia, or haemoconcentration, especially in dehydrated or systemically ill dogs (Davidson, 2003).Monitoring electrolyte status is crucial in dogs with DKA, as hypokalemia and hyponatremia are common (Nelson and Couto, 2014).

**Advanced Monitoring Tools**

Recent advances include continuous glucose monitoring systems (CGMS), which provide real-time interstitial glucose levels over several days (Gilor *et al*., 2016). These systems help identify glucose fluctuations and improve insulin dosing. Devices like FreeStyle Libre have shown promise in veterinary practice, although calibration remains essential (Corradini *et al.,* 2016). These methods are especially helpful in dogs with unpredictable glycemic patterns or unstable diabetes.

## TREATMENT STRATEGIES

**Insulin Therapy**

Exogenous insulin administration is the cornerstone of canine diabetes treatment (Nelson and Couto, 2014). Most dogs require twice-daily insulin injections to maintain glycemic control (Gilor *et al.*, 2016). The commonly used insulin types include intermediate-acting insulins like NPH and long-acting insulin preparations such as porcine lente (Rand *et al.,* 2004). Recently, insulin analogues like detemir and glargine have also been explored, although cost and hypoglycemia risk are concerns (Davison *et al.*, 2005).Selecting the appropriate insulin depends on the individual dog's response, owner compliance, and cost-effectiveness (Fleeman and Rand, 2001).

**Dietary Management**

Medical nutritional therapy is a vital adjunct to insulin in achieving glycemic control (Zini *et al.*, 2010). Diets high in fiber and complex carbohydrates slow glucose absorption and reduce postprandial spikes (Nelson, 2015). Consistency in feeding times and caloric intake is critical to prevent glucose fluctuations (Graham and Nelson, 2005).Protein-rich and low-fat diets are particularly important in diabetic dogs with concurrent pancreatitis or hyperlipidaemia (Catchpole *et al.*, 2005).

**Oral Hypoglycaemic Agents**

While not first-line therapy in dogs, oral hypoglycemics like sulfonylureas have shown limited efficacy (Mattin *et al.,* 2014). Dogs generally have insulin-dependent diabetes, making oral agents ineffective compared to cats (Hoenig, 2002). However, SGLT2 inhibitors and other newer classes are being evaluated experimentally in canine models (Gilor *et al.,* 2011).Research continues into the use of adjunctive oral therapies for insulin resistance or partial support in early disease.

**Management of Concurrent Illnesses**

Concurrent disorders such as pancreatitis, Cushing's disease, urinary tract infections, and obesity must be identified and addressed to ensure effective diabetic control (Feldman and Nelson, 2004). Treating these conditions may reduce insulin requirements and prevent glycemic instability (Nelson and Couto,, 2014).Frequent re-evaluations and a thorough systemic workup are recommended in poorly controlled diabetic dogs.

**Emergency Management of Diabetic Ketoacidosis (DKA)**

DKA is a life-threatening complication requiring prompt intravenous fluid therapy, regular insulin administration, and electrolyte correction (Wiedmeyer and Riches*,* 2008). Identification of precipitating causes (e.g., infection, insulin omission) is essential for resolution (Nelson, 2015). Serial monitoring of blood glucose, ketones, pH, and electrolytes is crucial during DKA therapy (Hess *et al*., 2000).

**MANAGEMENT AND MONITORING AT HOME**

**Importance of Owner Education and Compliance**

Successful long-term management of canine diabetes heavily depends on owner understanding and compliance (Fleeman and Rand*,* 2003). Pet owners must be trained in insulin administration, recognizing signs of hypoglycemia, and maintaining consistent feeding and exercise routines (Rand *et al*., 2004). Non-compliance is a major cause of unstable glycemic control (Nelson and Reusch, 2014).Educational tools and regular follow-ups help reinforce the importance of structured care at home (Gilor *et al.,* 2011).

### Monitoring Blood Glucose at Home

Home monitoring of blood glucose curves using glucometers validated for dogs allows real-time glycemic assessment (Zini *et al.*, 2009). This helps reduce stress hyperglycemia associated with in-hospital testing and provides more accurate data for insulin dose adjustments (Wess Reusch, 2000).Owners can be trained to perform capillary blood sampling from the ear or lip with minimal discomfort (Hess *et al.,* 2008).

### Urine Glucose and Ketone Testing

While not as precise as blood glucose, urine dipstick testing can serve as an auxiliary tool for detecting glucosuria or ketonuria (Nelson, 2015). Persistent glucosuria despite insulin treatment may indicate underdosing, whereas ketonuria may signal the onset of diabetic ketoacidosis (Wiedmeyer and Richese, 2008). Routine urine monitoring is especially useful in multi-pet households or when blood testing isn't feasible.

### Recognizing and Managing Hypoglycemia at Home

Hypoglycemia is the most common acute complication in diabetic dogs and is potentially life-threatening (Nelson, 2015). Owners should be trained to recognize signs such as weakness, tremors, seizures, or disorientation and administer oral glucose immediately (Gilor *et al*.,2016).If severe, the dog should be taken for emergency treatment involving IV dextrose and supportive care (Hess *et al.,* 2000).

### Lifestyle and Exercise Management

Regular, moderate exercise aids in glucose utilization and may help improve insulin sensitivity (Catchpole *et al.,* 2005). Sudden changes in exercise levels can, however, impact insulin requirements and should be avoided (Fleeman and Rand, 2001).Consistency is key in both timing and intensity of physical activity to maintain glycemic balance.

## COMPLICATIONS AND COMORBIDITIES

### Diabetic Ketoacidosis (DKA)

Diabetic ketoacidosis (DKA) is an acute, life-threatening complication resulting from insulin deficiency and counter-regulatory hormone excess (Nelson and Couto, 2014). It leads to hyperglycemia, ketonemia, and metabolic acidosis (Hess *et al.*, 2000). DKA is commonly triggered by infection, pancreatitis, or missed insulin doses (Wiedmeyer and Riches*,* 2008). Clinical signs include vomiting, anorexia, lethargy, dehydration, and fruity breath odor (Nelson, 2015). Prompt hospitalization, IV fluid therapy, insulin CRI, and electrolyte correction are essential (Feldman *et al.,* 2015).

### Hypoglycemia

Hypoglycemia can occur due to insulin overdose, inadequate food intake, or excessive exercise (Gilor *et al,* 2011). Signs include weakness, ataxia, disorientation, and seizures (Fleeman and Rand, 2001). Rapid

intervention with glucose administration is critical to prevent irreversible neurologic damage (Hess *et al.*, 2008).

### Cataracts and Vision Loss

Cataracts are a common chronic complication due to sorbitol accumulation within the lens from hyperglycemia (Gelatt *et al.*, 2006). More than 75% of diabetic dogs develop bilateral cataracts within 6–12 months of diagnosis (Beam *et al.,* 1999). Surgical removal via phacoemulsification can restore vision effectively if retinopathy is not present (Kern, 2007).

### Urinary Tract Infections

Persistent glucosuria promotes bacterial growth, predisposing dogs to urinary tract infections (UTIs) (Forrester *et al.,* 1990). Asymptomatic bacteriuria is common in diabetic dogs and may progress to pyelonephritis if untreated (Nelson and Couto, 2014). Routine urinalysis and culture are recommended during follow-ups (Fleeman and Rand*,* 2003).

### Pancreatitis and Other Endocrinopathies

Pancreatitis may be both a cause and consequence of diabetes mellitus, complicating insulin therapy and glucose control (Xenoulis *et al.,* 2008). Diabetic dogs are also at risk for concurrent endocrinopathies like Cushing's disease and hypothyroidism, which may alter insulin sensitivity (Catchpole *et al.,* 2005).

## PREVENTION AND RISK REDUCTION

### Early Identification of Predisposing Factors

Preventing diabetes in dogs begins with recognizing and mitigating modifiable risk factors such as obesity, chronic pancreatitis, and certain endocrinopathies (Catchpole *et al.,* 2008a). Breed predispositions, including in breeds like Miniature Schnauzers and Poodles, should prompt earlier screening (Mattin *et al.,* 2014). Monitoring for glucose intolerance in high-risk populations can enable earlier interventions (Fall *et al.*, 2008).

### Weight Management and Nutrition

Maintaining optimal body weight and avoiding excessive caloric intake can significantly reduce the risk of diabetes mellitus (Zini *et al.,* 2010). Feeding a balanced, portion-controlled diet with appropriate macronutrient content helps prevent obesity and insulin resistance (Behrend *et al.,* 2018). Owners should be educated about treats, table scraps, and high-glycemic foods (Graham *et al.,* 2017).

### Avoiding Diabetogenic Drugs

Long-term use of glucocorticoids and progestogens can lead to insulin resistance and eventual β-cell exhaustion (Nelson, 2015). Avoiding these medications in at-risk animals, or using them cautiously with proper monitoring, is advised (Feldman *et al.*, 2015).

### Regular Health Screening

Routine veterinary screening, including glucose, Fructosamine, urinalysis, and body condition scoring, helps identify diabetes at a subclinical stage (Tvarijonaviciute *et al.,* 2012). Dogs with concurrent conditions like hyperadrenocorticism or hypothyroidism should be monitored more frequently (Davison *et al.,* 2005).

### Genetic Counselling and Breeding Recommendations

Selective breeding to avoid propagation of genetic susceptibility is advised. Breeding of diabetic animals or close relatives should be discouraged (Davison *et al.*, 2007). Research suggests that autoimmunity and MHC class II alleles may play a role in certain breeds (Catchpole *et al*., 2008a).

## FUTURE DIRECTIONS AND RESEARCH GAPS

### Advances in Immunopathogenesis and Genetics

Emerging research is focusing on the immune-mediated mechanisms contributing to β-cell destruction in diabetic dogs, similar to type 1 diabetes in humans (Catchpole *et al.,* 2008b). Studies on MHC class II allele associations, particularly in breeds like the Samoyed and Cairn Terrier, suggest a genetic predisposition (Davison *et al.*, 2011). However, the exact immune triggers remain poorly defined, and further exploration into autoantibodies such as GAD65 and IA-2 is warranted (Davison *et al.,* 2008).

### Molecular Biomarkers and Early Diagnosis

New biomarkers including glycated albumin, adiponectin, GLP-1, and proinflammatory cytokines are being investigated for their role in early diagnosis and disease progression (Tvarijonaviciute *et al.*, 2012; Fracassi *et al.,* 2017). Non-invasive tests using saliva or urine metabolomics could transform early screening (Ferlizza *et al.,* 2015).

### Emerging Therapeutics: Beyond Insulin

Innovative treatments like GLP-1 receptor agonists, DPP-4 inhibitors, and SGLT2 inhibitors—widely used in human diabetes—are now being evaluated for veterinary use (Nelson *et al.*, 2021). Although insulin therapy remains the mainstay, alternative or adjunct therapies may improve glycemic control and reduce comorbid risks.

### Stem Cell and Regenerative Therapies

Research into pancreatic islet transplantation, mesenchymal stem cell therapy, and gene editing techniques offers hope for potential cures (Aragona *et al.*, 2020). However, species-specific challenges, ethical concerns, and cost factors hinder clinical application in veterinary practice.

**Technological Innovations and AI in Disease Monitoring**

The incorporation of continuous glucose monitoring systems (CGMS), telemonitoring, and AI-based insulin dosing algorithms is expected to revolutionize diabetes management (Cowie *et al.*, 2020). These technologies enhance owner compliance, improve clinical outcomes, and provide data-driven decision support for veterinarians.

## CONTROVERSIES IN TREATMENT OF CANINE DIABETES MELLITUS

**Insulin choice -traditional (lente/ PZI/NPH) vs long-acting analogues (glargine/detemir)** Many clinicians favour veterinary-licensed lente/PZI or NPH, while others advocate human analogues. Evidence on superiority is mixed (Behrend *et al.,* 2018; Rafferty and Reusch*,* 2022).

**Once-daily basal insulin protocols vs twice-daily regimens:** Some propose once-daily long-acting basal insulin (with/ without prandial doses), but others caution that BID dosing is more predictable in most dogs (Behrend *et al.*, 2018; Smith and O'Neill, 2020).

**Diet composition -low-carb vs high-fiber/moderate-carb diets:** While low-carb diets clearly aid remission in cats, the benefit in dogs is inconsistent — some studies show no advantage over standard diets (Johnson and Rand, 2008; Thomson *et al.*, 2010).

**Use of oral hypoglycaemic drugs in dogs:** Oral agents such as glipizide and metformin have limited and inconsistent evidence of benefit in dogs. Safety concerns — like lactic acidosis with metformin -limit their routine use (Adams and O'Neill, 2004; Brown and Reusch*.,* 2011).

**Adoption of continuous/flash glucose monitoring (CGM/FGM):** CGM/ FGM devices are increasingly used in dogs, raising debates about accuracy (especially at glucose extremes), sensor placement, interstitial vs blood glucose correlations, and cost-effectiveness (Johnson and Rand*,* 2016; Martinez *et al.,* 2018).

**Clinically relevant remission in dogs:** Remission is common in cats but considered uncommon in dogs. Case reports suggest it can occur, but the impact of treatment choices, diet, and monitoring intensity remains unclear (Thomson and Fleeman*,* 2016).

**New delivery systems -insulin pumps, pens, implants, and novel insulins:** These innovations (e.g., insulin pumps or ultra-long-acting analogues) promise fewer injections and smoother control, but their cost, availability, safety, and documented benefits in dogs remain under investigation (Rafferty and Reusch*,* 2022).

**How "tight" should glycaemic control be?** The balance between avoiding hyperglycaemia (to reduce complications) and preventing hypoglycaemia (which poses acute danger) is debated. Optimal target ranges and titration strategies in dogs

are not firmly established and may need individualization (Smith *et al.,* 2020).

## CONCLUSION

Canine diabetes mellitus is a complex and multifactorial endocrine disorder, most commonly resembling insulin-dependent diabetes mellitus in humans (Catchpole *et al.,* 2005). It arises due to destruction or dysfunction of pancreatic β-cells, often attributed to immune-mediated mechanisms or endocrinopathies (Guptill *et al.,* 2003).

The disease predominantly affects middle-aged to older, female dogs, with breed predispositions further emphasizing a strong genetic component (Mattin *et al.,* 2014). Diagnosis is based on clinical signs, persistent hyperglycemia, glucosuria, and exclusion of other endocrinopathies such as Cushing's disease (Rand *et al.,* 2004).

Despite being incurable, canine diabetes can be effectively managed through exogenous insulin therapy, nutritional modification, and regular monitoring of glycemic control (Nelson and Couto, 2014). Tools like continuous glucose monitoring systems (CGMS) and Fructosamine testing have improved management precision (Zini *et al.,* 2010).

Prognosis is favourable with early diagnosis, consistent therapy, and informed owner compliance (Gilor *et al.,* 2011). However, long-term complications such as cataracts, urinary tract infections, and diabetic ketoacidosis remain significant clinical concerns (Feldman and Nelson, 2004).

Recent advances in immunopathology, stem cell therapy, molecular biomarkers, and technology-based monitoring offer promising avenues for future research (Davison *et al.,* 2011; Cowie *et al.*, 2020). Continued efforts in early screening, risk factor modification, and personalized therapy protocols are essential for optimizing diabetic care in dogs (Catchpole *et al.,* 2008b).In summary, a multidisciplinary approach combining clinical vigilance, owner education, and research innovation is paramount to improving outcomes in canine diabetes mellitus.

## ACKNOWLEDGEMENT

The authors express their sincere gratitude to the faculties of Department of Veterinary Medicine, Veterinary College, Bengaluru, KVAFSU for their constant guidance, encouragement, and support during the preparation of this manuscript. The authors are also thankful to the library and information services of Veterinary College, Bengaluru for providing access to relevant scientific literature.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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