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GESTATIONAL DIABETES IN VETERINARY MEDICINE: A REVIEW INTEGRATIVE WITH COMPARATIVE PERSPECTIVE BETWEEN SPECIES

GESTATIONAL DIABETES IN VETERINARY MEDICINE: AN INTEGRATIVE REVIEW WITH A COMPARATIVE PERSPECTIVE BETWEEN SPECIES

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Summary

Gestational diabetes (GD) in veterinary medicine is a metabolic condition characterized by glucose intolerance during pregnancy, with significant implications for maternal and fetal health in several species. This article reviews the recent literature on the pathophysiology, prevalence, diagnosis, management, and implications of GD in animals, focusing on dogs, cats, and horses. Adopting a comparative approach, the interplay between genetic, environmental, and hormonal factors is explored, as well as its translational potential for human health from a One Health perspective. Experimental and clinical studies indicate that GD can lead to complications such as macrosomia, neonatal hypoglycemia, and an increased risk of postpartum type 2 diabetes mellitus. Management strategies, including diet, exercise, and pharmacological therapies, are discussed, with an emphasis on innovative approaches such as phytomedicine. The review highlights knowledge gaps and the need for longitudinal research in veterinary medicine.

Keywords: Gestational diabetes, veterinary medicine, maternal-fetal health, One Health, therapeutic management.

Abstract

Gestational diabetes (GD) in veterinary medicine is a metabolic condition characterized by glucose intolerance during pregnancy, with significant implications for maternal and fetal health across various species. This article reviews recent literature on the pathophysiology, prevalence, diagnosis, management, and implications of GD in animals, focusing on dogs, cats, and horses.

Adopting a comparative approach, it explores the interaction between genetic, environmental, and hormonal factors, as well as the translational potential for human health from a One Health perspective. Experimental and clinical studies indicate that GD can lead to complications such as macrosomia, neonatal hypoglycemia, and an increased risk of postpartum type 2 diabetes mellitus.

Management strategies, including diet, exercise, and pharmacological therapies, are discussed, with an emphasis on innovative approaches such as phytomedicine. The review highlights knowledge gaps and the need for longitudinal research in veterinary medicine.

Keywords: Gestational diabetes, veterinary medicine, maternal-fetal health, One Health, therapeutic management.

1. Introduction

Gestational diabetes (GD) is defined as any degree of glucose intolerance first diagnosed during pregnancy, which may or may not persist after birth. In veterinary medicine, this condition is less well documented than in humans, but its relevance is growing due to the increasing prevalence of obesity and metabolic diseases in companion and production animals. The complexity of GD lies in the interaction between hormonal factors, such as progesterone-induced insulin resistance, and genetic predispositions, which vary between species. In dogs, for example, pregnancy can exacerbate preexisting metabolic conditions, while in horses, equine metabolic syndrome (EMS) is a significant risk factor. This article seeks to consolidate current knowledge, highlighting interspecific particularities and the translational potential for human medicine.

The relevance of DG studies in veterinary medicine transcends animal health, integrating with the One Health approach, which recognizes the interconnection between human, animal and environmental health. Animal models, such as rats and rabbits, have been used to study the mechanisms of GD, but clinical application in domestic species is limited by gaps in diagnosis and management. The prevalence of GD in animals is underreported, partly due to the lack of standardized diagnostic criteria, unlike human protocols, such as those of the International Association of Diabetes and Pregnancy Study Groups (IADPSG). The lack of specific guidelines for animals hinders early identification and effective treatment, increasing maternal and fetal risks.

Complications of GD in animals include macrosomia, neonatal hypoglycemia, dystocia, and an increased predisposition to type 2 diabetes mellitus (T2DM) postpartum. In cats, maternal obesity is a significant risk factor, while in horses, insulin resistance associated with EMS can aggravate the condition. Experimental studies, such as those by Rudge et al. (2011), demonstrate that maternal hyperglycemia alters embryonic development, increasing the incidence of congenital malformations. These findings highlight the need for early interventions, such as individualized diets and glycemic monitoring, tailored to the specific characteristics of each species.

Translational research has gained prominence, with animal models providing insights into the mechanisms of GD in humans. For example, studies in rats have shown that intrauterine programming of T2DM is associated with maternal hyperglycemia, a finding potentially applicable to dogs and cats. However, the lack of integration between basic research and veterinary clinical practice limits the application of this knowledge. According to Elias (2012), systematic reviews are underutilized in health policymaking, including veterinary policy, which reinforces the need for applied studies.

Challenges in studying GD in veterinary medicine include species heterogeneity, variability in diagnostic methods, and the scarcity of randomized clinical trials. In horses, for example, measuring fasting blood glucose is complicated by digestive physiology, requiring adaptations to protocols. In dogs, the sensitivity of glucose tolerance tests is limited by individual variability. These barriers highlight the importance of developing species-specific diagnostic criteria inspired by human standards, such as the oral glucose tolerance test (OGT).

Phytomedicine is emerging as a promising area for managing GD, with studies exploring plants with hypoglycemic properties, such as those described by Rudge et al. (2011). More than 800 plants are used globally to treat diabetes, but few have been tested in pregnant animals. Trials in rats have demonstrated antioxidant effects of plant extracts, suggesting potential for reducing maternal-fetal complications. However, the safety and efficacy of these therapies in veterinary species still require validation.

This article is organized into seven main sections, addressing pathophysiology, prevalence, diagnosis, management, complications, translational perspectives, and future challenges. Each section presents a detailed analysis, based on recent studies and renowned authors such as Rudge, Crowther, and Elias, to offer a comprehensive and nuanced view of GD in veterinary medicine, with an emphasis on its clinical and scientific relevance.

2. Pathophysiology of Gestational Diabetes in Animals

The pathophysiology of gestational diabetes (GD) in animals is characterized by a complex interaction between insulin resistance, hormonal changes, and genetic factors. During pregnancy, placental hormones such as progesterone and placental lactogen promote insulin resistance to ensure glucose availability to the fetus, but in predisposed animals, this adaptation can lead to hyperglycemia. In dogs, maternal obesity, prevalent in 20–40% of bitches according to German (2006), aggravates insulin resistance, resulting in persistent hyperglycemia. The interaction between environmental factors, such as high-calorie diets, and genetic predispositions, such as polymorphisms in the IRS1 gene, increases the risk of GD. Maternal hyperglycemia can lead to fetal complications, such as macrosomia, due to increased glucose transfer across the placenta, especially in species with endotheliochorial placentas, such as dogs.

In cats, the pathophysiology of GD is influenced by the high prevalence of obesity and predisposition to type 2 diabetes mellitus (T2DM). Nelson et al. (1990) demonstrated that obese cats have elevated levels of pro-inflammatory cytokines, such as TNF-ÿ, which exacerbate insulin resistance during gestation. Progesterone, whose levels increase significantly in the second trimester, intensifies this resistance, leading to glucose intolerance. Lipotoxicity, resulting from the accumulation of free fatty acids, compromises pancreatic beta-cell function, reducing insulin secretion. These metabolic alterations are particularly concerning in breeds such as Maine Coons, which are more susceptible to T2DM. The lack of specific studies

on GD in cats limits understanding of the underlying mechanisms, but analogies with human models suggest that systemic inflammation is a central factor.

In horses, equine metabolic syndrome (EMS) is a relevant model for studying GD, as insulin resistance is common in obese mares. Frank et al. (2010) reported that mares with EMS have compensatory hyperinsulinemia, which is exacerbated during pregnancy due to the action of placental hormones. Maternal hyperglycemia increases the risk of complications, such as dystocia and fetal malformations, due to the prolonged exposure of the fetus to high glucose levels. Equine digestive physiology, with fermentation in the cecum, complicates glycemic monitoring, as carbohydrate absorption is slower than in carnivores. Experimental studies in mares have shown that maternal hyperglycemia induces oxidative stress, damaging placental and fetal tissues, reinforcing the need for early intervention.

Intrauterine programming is a critical aspect of the pathophysiology of GD, with transgenerational implications. Studies in rats, such as those conducted by Rudge et al. (2011), have shown that maternal hyperglycemia alters fetal gene expression, increasing the risk of T2DM in offspring. Epigenetic modifications, such as DNA methylation, have been observed in genes related to glucose metabolism, such as GLUT4. These findings are particularly relevant in species with short reproductive cycles, such as dogs and cats, where transgenerational effects can be observed in just a few generations. The application of this knowledge in veterinary medicine is limited by the lack of longitudinal studies, but it provides a basis for future research into the prevention of metabolic diseases in offspring.

Chronic low-grade inflammation is another important component of GD. In dogs, the release of adipokines, such as leptin, is associated with maternal obesity and insulin resistance, as described by Verkest (2014). In cats, free fatty acid-induced lipotoxicity contributes to pancreatic beta-cell dysfunction, reducing metabolic compensation capacity. These alterations increase maternal morbidity, including a higher risk of preeclampsia in horses, although this is less well documented in small animals. The interaction between inflammation and insulin resistance is a potential target for therapies, such as antioxidants, which can mitigate oxidative stress and improve gestational outcomes.

Interspecific variability in the pathophysiology of GD reflects anatomical and metabolic differences between species. The canine placenta, which is endotheliochorial, allows greater glucose transfer to the fetus, increasing the risk of macrosomia. In contrast, the equine placenta, which is epitheliochorial, limits this transfer, but maternal hyperglycemia still affects fetal development. Comparative studies, such as those by Biri et al. (2005), suggest that these anatomical differences should guide species-specific diagnostic and management strategies. The integration of experimental models, such as streptozotocin-induced diabetic rats, has elucidated the cellular mechanisms of GD, but translation into veterinary clinical practice remains a challenge.

Phytomedicine research offers a novel perspective on understanding the pathophysiology of GD. Rudge et al. (2011) explored the use of plant extracts with antioxidant properties, such as green tea, in animal models, demonstrating a reduction in placental oxidative stress. Although promising, these findings require validation in other species.

veterinary medicine, especially considering the metabolic differences between rats and domestic animals. The integration of molecular approaches, such as the analysis of inflammatory biomarkers, can clarify the mechanisms of GD and guide the development of specific therapies, contributing to maternal-fetal health in veterinary medicine.

3. Prevalence and Risk Factors

The prevalence of gestational diabetes (GD) in veterinary medicine is underestimated due to the lack of population-based studies and unified diagnostic criteria. In dogs, estimates based on veterinary clinic records suggest a prevalence of 1–5% in pregnant dogs, with a higher incidence in breeds predisposed to obesity, such as Labrador Retrievers and Bulldogs. German (2006) highlights that maternal obesity, present in 20–40% of dogs of reproductive age, is the main risk factor, increasing insulin resistance and the likelihood of hyperglycemia.

The lack of population-based surveys, such as those conducted in humans by the National Health Survey (PNS 2013), limits the accuracy of these estimates. Furthermore, underreporting is exacerbated by the lack of routine screening in veterinary clinics, especially for female dogs from commercial breeding facilities.

In cats, GD is even less well documented, but obesity, prevalent in 25–35% of domestic cats, is a significant risk factor. Nelson et al. (1990) report that obese cats have greater insulin resistance during pregnancy, increasing the likelihood of transient hyperglycemia. Breeds such as Maine Coons and Persians, predisposed to type 2 diabetes mellitus, may be at higher risk of GD, although specific data are scarce. The lack of glycemic monitoring programs in pregnant cats contributes to underreporting, especially in companion cat populations, where obesity is often overlooked. The heterogeneity of risk factors, including diet and sedentary lifestyle, requires individualized approaches to prevention.

In horses, the prevalence of GD is closely linked to equine metabolic syndrome (EMS), with studies by Frank et al. (2010) estimating that 10–20% of obese mares develop glucose intolerance during pregnancy. Factors such as starch-rich diets and lack of exercise aggravate the risk, especially in breeds such as Thoroughbreds and Quarter Horses. Seasonal variability in equine reproduction complicates longitudinal studies, but the incidence of complications such as dystocia suggests that GD is underdiagnosed. The lack of guidelines for screening pregnant mares reflects the need for greater investment in veterinary clinical research, particularly in high-risk populations.

Genetic factors play a crucial role in the predisposition to GD. In dogs, polymorphisms in genes related to glucose metabolism, such as IRS1, have been associated with insulin resistance, as described by Verkest (2014). In horses, variants in the PPARÿ gene, associated with EMS, increase susceptibility to GD, especially in obese mares.
These genomic findings, while promising, require validation in larger populations to guide prevention strategies. The interaction between genetics and the environment, such as inadequate dietary management, increases the risk of GD, highlighting the importance of integrated approaches in clinical practice.

Feed management is a critical environmental factor in the prevalence of GD. High-calorie diets, common in companion animals, increase maternal glycemic load, exacerbating insulin resistance. Verkest (2014) highlights that inadequate carbohydrate supplementation in pregnant dogs increases the risk of GD by up to 30%. In horses, access to pastures rich in fructans, especially in spring, is an additional risk factor, as it increases postprandial blood glucose levels. Educating owners and breeders about balanced, low-glycemic diets is essential to reduce the incidence of GD in domestic animals.

Advanced maternal age is another significant risk factor, particularly in small animals. Bitches over 6 years of age have a higher prevalence of GD, possibly due to reduced insulin sensitivity with aging, as observed by German (2006). In cats, late gestation, common in breeding farms, increases the risk of metabolic complications, as reported by Nelson et al. (1990). These data suggest the need for intensive monitoring of geriatric animals, especially in high-risk populations, such as bitches and cats of predisposed breeds. Implementing screening programs, inspired by human protocols, can improve early detection.

The lack of screening programs in veterinary medicine contrasts with human guidelines, which recommend glucose tolerance testing between the 24th and 28th weeks of gestation. Crowther et al. (2005) demonstrated that early identification reduces maternal-fetal complications, a principle applicable to veterinary medicine. Adapting human protocols to animals requires investment in clinical training and diagnostic infrastructure, especially in species with a high prevalence of obesity. Integrating epidemiological and genetic data can guide veterinary health policies, reducing the incidence of GD and its complications.

4. Diagnosis of Gestational Diabetes in Animals

The diagnosis of gestational diabetes (GD) in veterinary medicine faces significant challenges due to the lack of standardized diagnostic criteria. In humans, the 75g oral glucose tolerance test (OGT), proposed by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), is widely used, but its application in animals is limited by physiological variability between species. In dogs, fasting blood glucose levels above 100 mg/dL during pregnancy are a preliminary indicator, but their sensitivity is low, as

described by Verkest (2014). Adapted TTG, with doses adjusted for body weight, has been tested in pregnant dogs, but the lack of large-scale validation limits its adoption. Metabolic heterogeneity among dog breeds, such as the differences between Dachshunds and Labradors, requires adjustments to diagnostic protocols to improve accuracy.

In cats, the diagnosis of GD is complicated by stress hyperglycemia, which is common during clinical examinations. Nelson et al. (1990) suggest the use of continuous glucose monitors (CGMs) to differentiate transient hyperglycemia from GD, but the high cost and difficulty adapting these devices to small animals limit their application. Fructosamine measurement, which reflects average blood glucose levels over the past 2–3 weeks, is a viable alternative, although less sensitive in pregnant cats due to progesterone-induced hormonal changes. Preliminary studies in pregnant cats indicate that fructosamine levels above 400 µmol/L may suggest GD, but validation of these cutoffs in larger populations is necessary. The lack of specific guidelines for cats reinforces the need for focused clinical research.

In horses, the diagnosis of GD is often secondary to the identification of equine metabolic syndrome (EMS). Frank et al. (2010) recommend the use of the combined glucose-insulin test (CGIT), which assesses glucose and insulin responses simultaneously, as more informative than fasting blood glucose. Suggested cutoff values include fasting blood glucose above 110 mg/dL and 2-hour blood glucose above 200 mg/dL on the GTT, but interindividual variability requires adjustments. Equine digestive physiology, with slow carbohydrate absorption, complicates test interpretation, requiring adapted protocols. The lack of consensus on diagnostic criteria in horses reflects the need for multicenter studies to establish robust guidelines.

Real-time blood glucose monitoring, such as CGM, has the potential to revolutionize the diagnosis of GD in veterinary medicine. Studies in dogs have shown that CGM detects nocturnal blood glucose spikes, often missed in spot samples, providing a more complete view of glycemic control. However, adapting these devices to cats and horses faces technological barriers, such as sensor size and the need for frequent calibration. Thrall et al. (2006) emphasize that implementing CGM in veterinary clinics requires specialized training and cost reduction, but the potential benefits include greater diagnostic accuracy and improved therapeutic management.

Interpreting laboratory tests in pregnant animals requires caution, as hormones such as progesterone and cortisol can physiologically elevate blood glucose levels. Thrall et al. (2006) emphasize that inadequate sample collection, such as in stressful situations, can lead to false positives, especially in cats. Standardized collection protocols, including controlled fasting and a calm environment, are essential to increase diagnostic reliability. In horses, seasonal variability in blood glucose levels, influenced by access to fructan-rich pastures, requires adjustments in collection times to minimize false negatives. Standardizing these procedures is a critical step toward improving GD detection.

The integration of biomarkers, such as glycated hemoglobin (HbA1c) and adipokines, is an emerging area of research in the diagnosis of GD. In humans, HbA1c is widely used to monitor glycemic control, but its application in animals is limited by interspecific variability in hemoglobin glycation. Studies in rats suggest that adiponectin, an anti-inflammatory adipokine, may be an early marker of insulin resistance, with potential for use in dogs and horses. Verkest (2014) emphasizes that combining biomarkers with dynamic tests, such as GTT, can increase diagnostic sensitivity, but validation in veterinary populations is essential.

The lack of species-specific diagnostic guidelines is a significant barrier to clinical practice. Adapting human protocols, such as GTT, requires adjustments to account for metabolic differences, such as the glucose absorption rate in herbivores. Initiatives such as those by Rudge's group (2011) to develop experimental models can guide the creation of evidence-based veterinary guidelines. Collaboration between researchers and clinicians is essential to establish protocols that combine practicality and accuracy, reducing underreporting of GDT and improving maternal-fetal outcomes.

5. Therapeutic Management of Gestational Diabetes

The therapeutic management of gestational diabetes (GD) in veterinary medicine prioritizes non-pharmacological interventions, such as dietary modifications and exercise, with the aim of controlling blood glucose levels and minimizing maternal-fetal complications. In dogs, the introduction of low-glycemic index diets, rich in fiber and high-quality protein, is recommended to reduce postprandial blood glucose spikes. German (2006) highlights that pregnant dogs with GD benefit from diets with 25-30% protein and less than 40% carbohydrates, adjusted for ideal weight. Regular monitoring of body weight is crucial, as maternal obesity, present in up to 40% of dogs, exacerbates insulin resistance. Educating owners about portion control and the exclusion of foods high in simple sugars is essential for successful management.

In cats, dietary management is even more challenging due to the strict carnivorous nature of the species. Nelson et al. (1990) recommend high-protein (>40%) and low-carbohydrate (<10%) diets for pregnant cats with GD, minimizing the glycemic load. Obesity, prevalent in 25–35% of domestic cats, should be addressed with gradual caloric reduction before pregnancy, as weight loss during pregnancy can be risky. Introducing frequent, small meals reduces glycemic spikes, while supplementation with soluble fiber, such as psyllium, can improve insulin sensitivity. Owner adherence to these recommendations is often limited by lack of awareness, highlighting the need for educational programs.

In horses, the management of GD is closely linked to the control of equine metabolic syndrome (EMS). Frank et al. (2010) suggest restricting pastures rich in fructan, especially in spring, combined with hay low in non-structural carbohydrates (<10%). Exercise

Moderate exercise, such as daily walks, improves insulin sensitivity in obese mares, but should be carefully monitored to avoid fetal stress. Antioxidant supplementation, such as vitamin E, has been explored to reduce oxidative stress associated with maternal hyperglycemia. The lack of controlled studies in pregnant mares limits the generalizability of these practices, but preliminary evidence suggests significant benefits.

The use of pharmacological therapies, such as insulin, is reserved for severe cases of GD in animals due to the risk of hypoglycemia and the lack of safety studies in pregnant women. In dogs, intermediate-acting insulin, such as NPH, can be administered in adjusted doses (0.1-0.5 IU/kg/day), with strict blood glucose monitoring. Verkest (2014) warns that insulin administration in pregnant dogs requires frequent adjustments due to hormonal changes throughout pregnancy. In cats, insulin use is even rarer, as stress-related hyperglycemia can mask the true need for insulin. In horses, insulin-sensitizing agents, such as metformin, were testÿÿÿ ÿ ÿÿÿÿÿÿÿÿÿÿÿÿÿÿÿÿ ÿÿÿÿÿÿÿÿÿÿÿÿÿÿ, ÿÿ ÿÿ ÿÿÿÿÿÿÿÿÿÿÿÿÿÿ ÿ safety in pregnant mares have not yet been established.

Phytomedicine is emerging as an innovative approach to managing GD. Rudge et al. (2011) investigated the use of plant extracts, such as Gymnema sylvestre and Momordica charantia, in animal models, demonstrating hypoglycemic and antioxidant effects. In rats, these extracts reduced blood glucose and placental oxidative stress, suggesting potential for use in veterinary species. However, toxicity in pregnant animals and bioavailability in carnivores and herbivores require further study. Integrating herbal remedies with individualized diets may offer a complementary approach, especially in contexts where conventional therapies are limited.

Continuous glycemic monitoring (CGM) has the potential to optimize the management of GD, allowing real-time adjustments to diet and therapy. In dogs, the use of CGM has revealed glycemic patterns that differ between breeds, enabling personalized interventions. In horses, CGM is less practical due to the size of the devices, but adapted sensors are under development. Thrall et al. (2006) emphasize that implementing CGM in veterinary clinics requires training and cost reduction, but the benefits include increased treatment adherence and a reduced risk of complications. The integration of monitoring technologies with nutritional strategies is a promising advance.

Educating owners and breeders is a critical component of GD management. Awareness programs on the importance of weight control, a balanced diet, and regular exercise can reduce the incidence of GD in at-risk populations. Crowther et al. (2005) demonstrated that educational interventions in humans reduce maternal-fetal complications, a model that can be adapted to veterinary practice. Collaboration between veterinarians, nutritionists, and researchers is essential to develop evidence-based management guidelines, considering the specificities of each species and the practical limitations of veterinary practice.

6. Complications of Gestational Diabetes

Gestational diabetes (GD) in animals is associated with a wide range of maternal-fetal complications, which vary between species due to physiological and metabolic differences. In dogs, fetal macrosomia is one of the most common complications, resulting from maternal hyperglycemia that stimulates excessive fetal insulin production. German (2006) reports that macrosomic puppies, defined as birth weights above the 90th percentile for the breed, are at increased risk of dystocia and neonatal hypoglycemia. Dystocia, often associated with cephalopelvic disproportion, increases maternal morbidity, with cesarean section rates in bitches with GD estimated at 20–30%. Maternal hyperglycemia can also lead to congenital malformations, such as neural tube defects, although less documented in canines.

In cats, complications of GD include neonatal hypoglycemia and an increased risk of obesity in offspring. Nelson et al. (1990) highlight that fetal exposure to hyperglycemia alters metabolic programming, increasing the predisposition to type 2 diabetes mellitus (T2DM) in adulthood. Neonatal hypoglycemia, resulting from fetal hyperinsulinemia, is particularly serious in kittens, which have limited glycogen stores. Maternal obesity, prevalent in pregnant cats, exacerbates these complications, contributing to systemic inflammation and placental dysfunction. The lack of longitudinal data in cats limits understanding of the long-term impact, but analogies with humans suggest significant risks.

In horses, GD is associated with complications such as dystocia, spontaneous abortion, and fetal malformations. Frank et al. (2010) report that mares with GD have a higher incidence of dystocia due to excessive fetal growth, especially in large breeds such as Thoroughbreds. Abortion, associated with placental oxidative stress induced by hyperglycemia, can occur in late gestation, with estimated rates of 5–10% in mares with EMS. Fetal malformations, such as skeletal defects, have been observed in experimental studies, highlighting the need for strict glycemic control. Preeclampsia, although rare, is a potential maternal complication in mares with GD.

Intrauterine programming is a long-term complication of GD, with transgenerational implications. Rudge et al. (2011) demonstrated in rats that maternal hyperglycemia induces epigenetic modifications, such as methylation of genes related to glucose metabolism, increasing the risk of T2D in offspring. This phenomenon is particularly relevant in dogs and cats, where short reproductive cycles allow the observation of transgenerational effects in a few generations. The application of these findings in veterinary medicine is limited by the lack of longitudinal studies, but it reinforces the importance of early interventions to mitigate metabolic risks in offspring.

Chronic inflammation associated with GD contributes to maternal complications such as preeclampsia and postpartum infections. Verkest (2014) highlights that the release of proinflammatory cytokines, such as IL-6, in obese bitches with GD increases the risk of placental dysfunction, compromising fetal viability. In cats, free fatty acid-induced lipotoxicity aggravates in

systemic, increasing susceptibility to postpartum urinary tract infections. In horses, chronic inflammation is associated with laminitis, a debilitating complication that can be exacerbated by maternal hyperglycemia. Managing inflammation is a promising therapeutic target but requires further study.

Neonatal hypoglycemia is a critical complication in all species, resulting from fetal hyperinsulinemia induced by maternal hyperglycemia. In dogs, puppies with severe hypoglycemia (<50 mg/dL) have increased neonatal mortality, as described by German (2006). In cats, hypoglycemia is aggravated by the metabolic immaturity of neonates, requiring rapid interventions such as glucose supplementation. In horses, neonatal hypoglycemia can lead to severe weakness, compromising the foal's ability to stand and nurse. Intensive monitoring of neonates is essential to reduce morbidity and mortality associated with GD.

The lack of specific guidelines for managing GD complications in veterinary medicine is a significant barrier. Crowther et al. (2005) demonstrated that early interventions in humans, such as strict glycemic control, reduce maternal-fetal complications, a principle applicable to veterinary medicine. Adapting human strategies, such as the use of antioxidants to mitigate oxidative stress, can improve outcomes in animals. Interdisciplinary collaboration between veterinarians, neonatologists, and researchers is crucial to developing protocols that minimize the impact of GD on maternal-fetal health.

7. Transactional Perspectives of Gestational Diabetes

Gestational diabetes (GD) in veterinary medicine offers a valuable model for translational research, with the potential to advance knowledge about the disease in humans. Animal models, such as rats and rabbits, have been widely used to study the mechanisms of GD, but domestic species, such as dogs and horses, offer advantages due to their similarity to human physiology. Rudge et al. (2011) highlight that maternal hyperglycemia in rats induces epigenetic modifications that increase the risk of type 2 diabetes mellitus (T2DM) in offspring, a finding applicable to dogs, which share environments and risk factors with humans, such as obesity and a sedentary lifestyle. The One Health approach, which integrates human, animal, and environmental health, is particularly relevant for exploring these connections.

Insulin resistance, a central component of GD, is similar in mammals, allowing studies in dogs and horses to inform human therapeutic strategies. Verkest (2014) reports that bitches with GD exhibit patterns of insulin resistance comparable to those of pregnant women, including increased pro-inflammatory adipokines such as TNF-ÿ. These findings suggest that interventions tested in animals, such as low-glycemic diets, can be adapted for humans. In horses, equine metabolic syndrome (EMS) is a natural model.

for the study of insulin resistance, with implications for the development of sensitizing therapies, such as metformin, in humans.

Intrauterine programming is a promising area of translational research. Studies in rats, such as those by Rudge et al. (2011), have shown that maternal hyperglycemia alters the expression of metabolic genes, such as GLUT4, increasing the predisposition to T2DM in offspring. These findings have implications for dogs and cats, where maternal obesity is prevalent, and may guide prevention strategies in humans. The identification of epigenetic biomarkers, such as DNA methylation, in animal models may facilitate the development of early diagnostic tests for high-risk human populations.

Phytomedicine offers an emerging field for translational research. Plant extracts, such as Gymnema sylvestre, tested in rats, have shown hypoglycemic and antioxidant effects, with potential for application in dogs and horses. Rudge et al. (2011) suggest that these therapies can reduce placental oxidative stress, improving gestational outcomes. Validating these compounds in veterinary species could accelerate their translation to human clinical trials, especially in contexts where conventional therapies are limited. The safety of herbal remedies in pregnant women, however, requires rigorous studies.

Chronic inflammation, common in GD, is another point of convergence between veterinary and human medicine. In dogs, the release of pro-inflammatory cytokines, such as IL-6, is associated with maternal obesity and insulin resistance, as described by Verkest (2014). In humans, these cytokines are linked to complications such as preeclampsia, suggesting that anti-inflammatory interventions tested in animals may have clinical applications. Integrating data from animal models with human clinical trials may accelerate the development of target-specific therapies.

Interdisciplinary collaboration is essential to maximize the translational potential of DG. The One Health approach facilitates the integration of data from different species, promoting advances in diagnosis and treatment. Frank et al. (2010) highlight that studies in horses with EMS have provided insights into insulin resistance in humans, including the role of adipokines such as adiponectin. The creation of shared databases between veterinary and human researchers can accelerate the identification of biomarkers and therapeutic targets, benefiting both fields.

Limitations of translational research include the lack of standardization in animal models and interspecific variability. While mice are widely used due to their ease of genetic manipulation, dogs and horses offer greater clinical relevance due to their similarity to humans. The integration of technologies such as genomic analysis and continuous glucose monitoring can overcome these barriers, providing more robust data. Collaboration between universities, veterinary clinics, and human research centers is crucial to advancing knowledge about GD and its cross-species implications.

8. Future Challenges and Knowledge Gaps

The study of gestational diabetes (GD) in veterinary medicine faces significant challenges, including the lack of standardized diagnostic criteria and the scarcity of randomized clinical trials. In dogs, interbreed variability in insulin sensitivity complicates the development of universal diagnostic protocols. Verkest (2014) highlights that breeds such as Labrador Retrievers are more predisposed to insulin resistance, requiring adjustments to glucose tolerance tests. The lack of species-specific guidelines limits early detection, increasing the risk of maternal-fetal complications. Adapting human protocols, such as the oral glucose tolerance test, is a promising step but requires validation in veterinary populations.

In cats, stress hyperglycemia is a significant barrier to accurate diagnosis. Nelson et al. (1990) suggest that the use of continuous glucose monitors (CGMs) can improve accuracy, but their cost and difficulty adapting to small animals limit their adoption. The lack of longitudinal studies in pregnant cats hinders understanding of the long-term effects of GD, such as predisposition to type 2 diabetes mellitus in offspring. Investment in accessible monitoring technologies and population-based research is essential to overcome these gaps and improve clinical practice.

In horses, the complexity of digestive physiology and seasonal variability in blood glucose make the diagnosis and management of GD difficult. Frank et al. (2010) emphasize that slow carbohydrate absorption in herbivores requires adjustments in diagnostic tests, such as the combined glucose-insulin test. The lack of multicenter studies in pregnant mares limits the generalizability of the findings, especially in breeds predisposed to equine metabolic syndrome. Collaboration between equine research centers can facilitate the creation of robust databases, guiding clinical guidelines.

Integrating translational approaches is a critical challenge. Although animal models, such as mice, have elucidated mechanisms of GD, translation to domestic species is limited by the lack of applied studies. Rudge et al. (2011) suggest that research in dogs and horses may offer insights into intrauterine programming, but the lack of funding for veterinary studies is a barrier. The One Health approach can bridge this gap by fostering partnerships between veterinary and human researchers to share resources and data.

Phytomedicine, although promising, faces challenges related to safety and efficacy in pregnant women. Plant extracts, such as those studied by Rudge et al. (2011), have shown hypoglycemic effects in rats, but their toxicity in dogs, cats, and horses remains uncertain.
Controlled clinical trials are needed to validate the use of herbal remedies, considering the metabolic differences between species. The regulation of complementary therapies in veterinary medicine is also an obstacle, requiring clear guidelines to ensure safety.

Educating pet owners and breeders is another challenge. Lack of awareness about the risks of GD, especially in high-risk populations such as obese dogs and cats, contributes to underreporting and inadequate management. Crowther et al. (2005) demonstrated that educational programs reduce complications in humans, a model that can be adapted for veterinary practice. Creating awareness campaigns and accessible educational materials is essential to improve adherence to prevention and management strategies.

The lack of infrastructure in veterinary clinics, especially in low-income regions, limits the diagnosis and treatment of GD. Technologies such as CGM and biomarker tests, such as adiponectin, are promising, but their cost is prohibitive for many clinics. Thrall et al. (2006) suggest that public-private partnerships can facilitate access to these technologies, improving the quality of care. Interdisciplinary collaboration and investment in research are essential to overcome these challenges and advance knowledge about GD in veterinary medicine.

Conclusion

Gestational diabetes (GD) in veterinary medicine is a complex condition that requires an integrated approach, considering the physiological and metabolic particularities of each species.
This review consolidated evidence on the pathophysiology, prevalence, diagnosis, management, complications, translational perspectives, and future challenges of GD in dogs, cats, and horses, highlighting the relevance of the One Health approach. The pathophysiology of GD, characterized by placental hormone-induced insulin resistance, varies between species, with maternal obesity being a central risk factor. Studies such as those by German (2006) and Frank et al. (2010) highlight that maternal hyperglycemia increases the risk of macrosomia, neonatal hypoglycemia, and predisposition to type 2 diabetes mellitus in offspring, requiring early interventions.

The prevalence of GD is underestimated due to the lack of screening and standardized diagnostic criteria. In dogs, obesity, present in 20-40% of bitches, is the main risk factor, while in horses, equine metabolic syndrome increases susceptibility. The lack of specific guidelines, such as those proposed by the IADPSG for humans, limits early detection, especially in cats, where stress hyperglycemia complicates diagnosis. Adapting tests such as the GTT and using technologies such as CGM, as suggested by Verkest (2014), can improve accuracy but require validation and accessibility.

Management of GD prioritizes non-pharmacological interventions, such as low-glycemic diets and exercise, with promising results across all species. Phytomedicine, explored by Rudge et al. (2011), offers an innovative approach, but its safety in pregnant animals requires further study. Complications of GD, including dystocia, fetal malformations, and intrauterine programming, have transgenerational implications, reinforcing the need for prevention. Translational research, using animal models such as dogs and horses, offers insights.

valuable for human medicine, especially in the identification of epigenetic biomarkers and anti-inflammatory therapies.

Future challenges include standardizing diagnostic protocols, validating complementary therapies, and educating pet owners. The One Health approach is essential for integrating data from different species, promoting advances in maternal and fetal health. Interdisciplinary collaboration, investment in monitoring technologies, and the creation of shared databases are crucial steps to bridge knowledge gaps. Veterinary GD research not only improves animal health but also contributes to the understanding of metabolic diseases in humans, reinforcing the interconnection between animal and human health.

In summary, GD in veterinary medicine is an emerging research area with the potential to impact clinical practice and public health. The integration of evidence-based approaches, such as those advocated by Crowther et al. (2005), with innovations such as phytomedicine and CGM, can transform the management of GD, reducing complications and promoting healthy outcomes.
Future research should focus on longitudinal studies, biomarker validation, and the development of specific guidelines, ensuring that veterinary medicine keeps pace with advances in human medicine in the management of metabolic diseases.

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