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From fat to facts: the potential of adipokine and insulin dosing in obese feline patients

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The increasing prevalence of obesity in domestic cats is closely linked to the emergence of diabetes mellitus, highlighting the need for early diagnostic tools. Obese cats typically show elevated leptin and reduced adiponectin levels—markers associated with early insulin resistance. Leptin resistance and compensatory hyperinsulinemia further reflect early metabolic dysfunction. These endocrine changes mirror those seen in humans and dogs, suggesting shared mechanisms across species. Incorporating these biomarkers into clinical practice could aid early risk stratification and preventive care. However, standardized reference ranges and cost-effective assays are still needed. This review assesses the predictive value of adiponectin, leptin, and insulin in identifying diabetes risk in obese cats.

KEYWORDS

feline obesity, adiponectin, leptin, insulin, diabetes mellitus, adipokines

1 Introduction

Obesity is an increasingly common and serious health concern in domestic cats, with reported prevalence ranging from 11.5% to 63% worldwide (Antakyalioglu et al., 2024; Tarkošová et al., 2016). This condition contributes to a range of comorbidities, most notably osteoarthritis and diabetes mellitus (DM), both of which significantly impair quality of life and longevity. Metabolic dysfunction associated with excess adipose tissue, particularly adipokine imbalance marked by increased leptin and decreased adiponectin, plays a central role in the development of insulin resistance and related disorders (Stenberg et al., 2023; Araújo et al., 2024).

Among the biomarkers associated with metabolic regulation, the leptin-to-adiponectin ratio (LAR) has gained attention as a sensitive indicator of insulin resistance and metabolic imbalance across species, including felines (Öhlund et al., 2018). Leptin, secreted in proportion to fat mass, regulates energy balance by signaling satiety to the hypothalamus, while adiponectin enhances insulin sensitivity and exerts anti-inflammatory effects (O'Neill et al., 2016; Nelson and Reusch, 2014). In obese cats, elevated leptin levels and reduced adiponectin concentrations result in a higher LAR, reflecting diminished leptin responsiveness and an inflammatory state that predisposes to diabetes mellitus (O'Neill et al., 2016; Araújo et al., 2024).

Beyond metabolic implications, obesity can also exacerbate orthopedic and cardiovascular complications, including limited mobility, hypertension, and increased heart rate (Sandøe et al., 2014; Clark and Hoenig, 2021; Souza et al., 2020; Rodan and Ellis, 2013). These multifaceted effects emphasize the need for integrated weight-management strategies and owner education regarding the consequences of feline obesity (Vitor et al., 2024; Klotsman et al., 2021).

This review critically examines the diagnostic and predictive potential of three key biomarkers: insulin, leptin, and adiponectin, in the context of feline obesity and diabetes. By synthesizing current evidence on their interplay and clinical utility, we aim to inform the development of early detection strategies and targeted interventions to reduce diabetes risk in feline patients.

1.1 Search strategy

A comprehensive narrative literature search was performed using the following databases: PubMed, Scopus, Web of Science, VetMed Resource, and PubMed Central. The search targeted open access publications published between 2000 and 2024, focusing on peer-reviewed studies relevant to feline obesity and metabolic health. The following keyword combinations were used: feline obesity, cat nutrition, leptin, adiponectin, energy balance, high-protein diet, feline metabolic health, body composition, inflammation markers, and dietary management. Only articles involving domestic cats were included, although comparative data from other species were considered when they offered translational value. Studies were selected based on their relevance, clarity of methodology, and direct contribution to understanding the physiological, nutritional, and endocrine mechanisms involved in feline obesity and diabetes risk. No formal quality scoring tools were applied, as this was not a systematic review.

2 Obesity in feline patients: epidemiology and health implications

2.1 Prevalence of obesity in cats

The prevalence of overweight and obese cats has increased dramatically, according to several studies. Depending on the population and geographic area, estimates range from 11.5% to 63% of cats being overweight or obese (Tarkošová et al., 2016). This pattern is indicative of a larger epidemic where weight growth has been influenced by environmental and lifestyle variables, much like what has been seen in human populations. Studies conducted in the UK have shown that between 40% and 52% of pet cats are obese, especially indoor cats who are less active (Courcier et al., 2010; Courcier et al., 2012). Reduced physical activity, higher calorie intake, and shifting owner conceptions of the ideal body condition have all been linked to the rising trend of obesity in cats (Phillips et al., 2017; Courcier et al., 2010; Mori et al., 2016). In particular, owners frequently ignore excess weight because they find larger cats

charming or attractive, which can cause those pets to gain more weight (Mori et al., 2016).

Furthermore, it has been proposed that the COVID-19 pandemic made the problem of feline obesity worse, with reports showing a rise in weight-related problems when pet owners changed their feeding schedules and spent more time at home (Machado et al., 2022). Cat obesity rates were shown to have increased as a result of this modification and fewer exercise chances during lockdowns, which highlights the necessity of focused weight management programs at veterinary clinics (Machado et al., 2022).

The growing frequency of obesity in cats has notable consequences since being overweight is connected to several health problems, including respiratory diseases, osteoarthritis, and diabetes mellitus (Loftus and Wakshlag, 2014). This underlines how urgently veterinary practitioners must provide obesity control and preventive strategies, including nutrition advice, exercise recommendations and owner education.

2.2 Causes of obesity in cats

Genetic predisposition greatly affects the course of obesity in cats. Studies indicate that variations in their endocrine and metabolic systems might lead to some breeds to be susceptible to obesity. Heritability factors linked to body weight and fat deposition show this genetic influence, suggesting that obesity may be partially inherited (Wallis and Raffan, 2020; Bairqdar et al., 2023). The importance of genetics in obesity susceptibility has been highlighted by the discovery that certain genetic variants are connected to body fat distribution and metabolism (Bairqdar et al., 2023; Hastuti, 2022). Some cats can also be genetically inclined to insulin resistance, which could aggravate weight gain, and the development of diseases related to obesity (Wallis and Raffan, 2020).

One of the main causes of feline obesity is environmental factors. Compared to their outdoor counterparts, cats who live indoors have fewer opportunities for physical activity, which frequently results in inactive lifestyles. Indoor cats are more likely to be obese because they participate less in exercise-promoting natural hunting activities (Stenberg et al., 2023; Arena et al., 2021). Moreover, a cat's degree of activity and therefore its body weight may be influenced by elements such the number of pets and the daily human interaction time (Teng et al., 2020; Godfrey et al., 2024). Factors include housing space, the accessibility of interesting toys, and opportunities for environmental enrichment also affect a cat's overall activity and metabolism (Lawson et al., 2019).

Cat obesity is directly caused by diet, which includes feeding habits in addition to the type and amount of food consumed. Ad libitum (free feeding) cats frequently eat too many calories, which causes them to gain weight (Rollins and Murphy, 2019). It has also been demonstrated that body weight and fat formation are influenced by the macronutrient composition of their food, particularly the proportion of proteins to carbs (Li and Pan, 2020; Goloni et al., 2024). Changed gut microbiota patterns observed in

obese cats could make weight control efforts more difficult by influencing how energy is drawn from diet (Kieler et al., 2015; Ma et al., 2022). The link between certain dietary practices, such as high starch consumption, and challenges controlling weight in neutered cats (Hoenig et al., 2003; Goloni et al., 2024; Saavedra et al., 2024) underlines the need for post-surgical food management in avoiding obesity. Overeating and treat distribution can also cause too much calorie intake, which increases the likelihood of obesity (Lackey et al., 2016; Lawson et al., 2019).

2.3 Consequences of obesity

Cat obesity has a major negative effect on their health, leading to a number of issues that shorten their lifespan and negatively impact on their general well-being.

2.3.1 Insulin resistance

The increased risk of diabetes mellitus is one of the most serious effects of obesity. Chronically high blood glucose levels are the result of insulin resistance, which is caused by excess body fat and impairs the body's ability to respond to insulin (Hoelmkjaer et al., 2016). Research shows that cats who are obese are far more likely to develop type 2 diabetes, and their insulin sensitivity decreases by 30% for every kilogram of body weight (Kocabağlı et al., 2017; Clark and Hoenig, 2021). These animals' metabolic dysfunction is characterized by a combination of insulin resistance and glucotoxicity, which, if left untreated, can result in serious diabetes consequences (Lewitt et al., 2016; Clark and Hoenig, 2021; Martin and Wood, 2010).

Many studies have shown that overweight cats have higher fasting insulin levels, implying this issue (Vitor et al., 2024; Appleton et al., 2000b; Zapata et al., 2017; Hoelmkjaer et al., 2016). As a result, these cats could struggle to keep appropriate glucose homeostasis, which could influence their diabetes mellitus risk, a condition defined by consistently elevated blood sugar levels caused by insulin resistance. Recent research has revealed the processes behind the link between obesity and insulin resistance, especially in cats. For instance, Hoenig et al. found that, particularly in older populations, overweight cats show significant changes in postprandial glucose metabolism and decreased insulin sensitivity (Hoenig et al., 2011a). This is corroborated by Vitor et al., who found that in obese cats, higher blood glucose levels are correlated with higher body condition scores (Vitor et al., 2024; Lewitt et al., 2016). The dysregulation of glucose metabolism is exacerbated by changes in the secretion of adipokines, such as leptin and adiponectin, which are implicated in insulin signaling (Araújo et al., 2024; Takashima et al., 2016).

This interaction highlights how complicated cat metabolism is, especially when it comes to obesity and food composition. Being genuine carnivores, cats naturally consume a diet low in carbs and rich in protein. Due to unnatural nutritional constraints, insulin dynamics may be negatively altered by diets high in carbs, which can result in a reduction in insulin sensitivity (Brearley et al., 2006; Hoenig et al., 2007).

2.3.2 Liver dysfunction

Furthermore, liver illness, especially hepatic lipidosis, which can happen when excessive fat buildup overtakes liver function, is closely associated with obesity in cats (Tarkošová et al., 2016). Because the liver cannot process fat effectively, fat increases and causes hepatic dysfunction, this condition is significantly more common in overweight and obese cats. Liver disease can have serious effects, including increased death rates and multi-organ dysfunction in cats (Tarkošová et al., 2016; Bjørnvad and Hoelmkjaer, 2014).

2.3.3 Joint disease

Reduced mobility and joint issues are also associated with obesity. Cats who are overweight are more likely to develop degenerative joint disease and lameness because of the increased stress on their joints (Maniaki et al., 2021; Bjørnvad and Hoelmkjaer, 2014). This disease is particularly worrisome since it produces persistent pain as well as decreases a cat's activity level, hence aggravating obesity by decreasing exercise (Bjørnvad and Hoelmkjaer, 2014). Additionally, because obesity alters body composition and fat distribution, research has suggested a potential link between obesity and a higher prevalence of dermatological conditions and lower urinary tract issues (Tarkošová et al., 2016).

3 Relevance of adipokines

Important fat metabolism regulators in the context of obesity, adipokines are bioactive chemicals secreted by adipose tissue that control several metabolic processes. Among these peptides, leptin and adiponectin influence insulin sensitivity, inflammation, energy expenditure, and appetite control (Arner, 2005; Blüher and Schwarz, 2014; Blüher, 2012; Park and Shimokawa, 2024; Gupta et al., 2024). Dysregulation of adipokine secretion in obese people relates to metabolic disorders, such insulin resistance and type 2 diabetes, thereby emphasizing their clinical value (Abed et al., 2023; Armstrong et al., 2011; Andrade-Oliveira et al., 2015).

Leptin regulates energy expenditure and appetite. Obese cats, on the other hand, often exhibit leptin resistance, characterized by greater serum levels but lesser responsiveness, which helps to preserve weight (Appleton et al., 2002). Studies reveal that obese cats have reduced adiponectin levels; its decline links with obesity and may aggravate insulin resistance and inflammatory responses, typical of obesity-related issues (Ishioka et al., 2009; Zapata et al., 2017). Changes in these signaling molecules synthesis in cats have been linked to the emergence of obesity-related conditions such diabetes and heart disease (Ishiooka et al., 2009; Okada et al., 2019; Kim et al., 2023; Corvera, 2021). Additionally, adipokines systemic impact is demonstrated by the inter-organ communication they facilitate, which impacts not just adipose tissue but also muscle, liver, and vascular functions (Korek and Krauss, 2015; Dongre, 2021; Gupta et al., 2024). The underlying mechanism is illustrated in Figure 1, which provides a detailed explanation of its components and how they interact. Given the striking similarity of this trend to findings in people, cats are a great model for research on metabolic diseases connected to obesity (Velde et al., 2013).
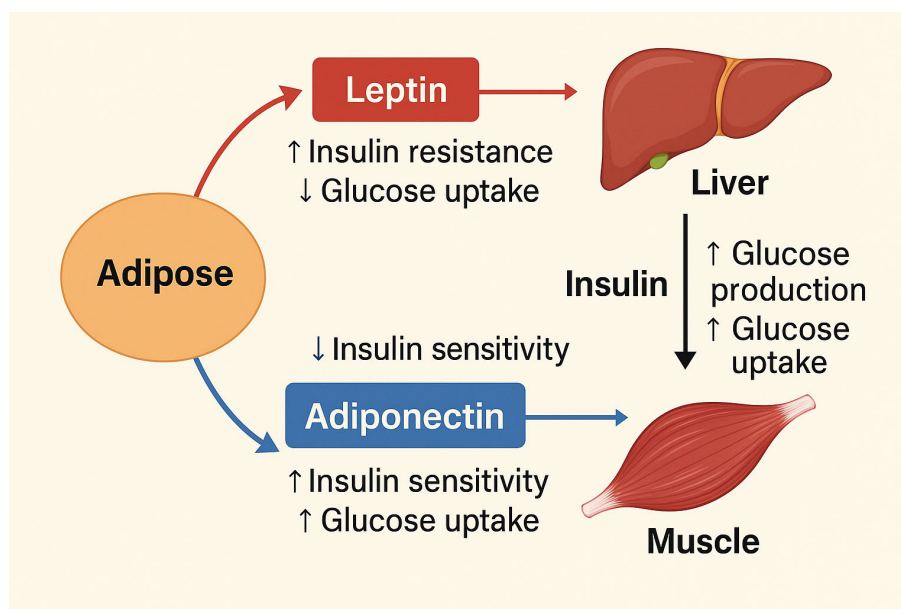
FIGURE 1
Descriptive diagram of adipose tissue, leptin, adiponectin and insulin.

3.1 Adipokines: key regulators of fat metabolism

3.1.1 Leptin

Leptin is a vital adipokine that is mostly secreted by adipose tissue and is necessary for regulating energy balance, metabolism, and appetite (Lee et al., 2007). It is essential for maintaining body weight homeostasis, and it is more prevalent in obese individuals, including cats (Takashima et al., 2016). Because it informs the hypothalamus about the condition of energy storage, leptin plays a crucial role in reducing appetite and raising energy expenditure (Zhao et al., 2019).

Because of the expansion of fat tissue, leptin levels usually increase when a cat is obese; it has also been shown to be positively related with body weight, body condition score, and body fat percentage (Vester et al., 2011). These relationships show leptin's dual role as metabolic control and a sign of obesity. According to one study, overweight cats have greater leptin levels and acquire a kind of leptin resistance comparable to that seen in overweight humans (Lee et al., 2007; Appleton et al., 2000b). Hyperleptinemia is a condition in which high amounts of circulating leptin do not sufficiently control weight or decrease hunger (Sharma and Sharma, 2018). Apart from its connection to energy metabolism, leptin exhibits pro-inflammatory properties that may aggravate chronic inflammation caused by obesity (Booth et al., 2016; Araújo et al., 2024). Increased production of pro-inflammatory cytokines by macrophages and other immune cells infiltrating adipose tissue in obese individuals can worsen insulin resistance and metabolic dysfunction (Araújo et al., 2024). Furthermore, because of its interactions with other hormonal pathways, particularly its role in controlling insulin sensitivity, leptin is seen as a key factor in the evolution of obesity-related comorbidities such diabetes mellitus (Takashima et al., 2016).

3.1.2 Adiponectin

Adiponectin is an important adipokine that regulates insulin sensitivity and metabolic health. It also has a big impact on feline obesity. Adiponectin, which is mostly secreted by adipose tissue, comes in a variety of forms (Frank and Walsh, 2017; Hoenig et al., 2011a; Takashima et al., 2016).

Studies revealing that adiponectin levels directly correlate with metabolic health in lean cats and obese cats have far lower circulating levels of adiponectin than cats with a lower body condition score (Tvarijonaviciute et al., 2012; Öhlund et al., 2015; Hoenig et al., 2013). Insulin resistance, a risk factor for diabetes mellitus, can result from this decreased adiponectin secretion (Öhlund et al., 2015; Hoenig et al., 2013).

On the other hand, reduced adiponectin levels in obesity are associated with higher inflammatory marker levels and impaired lipid metabolism, which exacerbates insulin resistance (Hoenig et al., 2013; Stenberg et al., 2023). Interestingly, research indicates that overweight cats who lose weight have more adiponectin, suggesting that weight loss efforts could help to correct certain metabolic anomalies (Takashima et al., 2016; Hoenig et al., 2013).

3.1.3 Insulin

Like other species, insulin is necessary for energy homeostasis and glucose metabolism in cats. In cats, insulin sensitivity and glucose tolerance are significantly influenced by body weight and obesity; these two parameters are intimately linked to insulin secretion and action. The dysregulation of insulin is a critical factor in the development of metabolic disorders in obese cats, as it is a critical regulator of glucose metabolism (Strage et al., 2021). In these animals, an increase in adiposity is closely linked to a decrease in insulin sensitivity, which results in a compensatory increase in pancreatic insulin secretion. This hyperinsulinemia frequently

serves as an early indicator of metabolic dysfunction, occurring prior to the development of overt hyperglycemia and clinical diabetes mellitus (Clark and Hoenig, 2021; Appleton et al., 2000b).

Research has particularly revealed that every kilo of body weight correlates to a notable drop in insulin sensitivity (Clark and Hoenig, 2021). Emphasizing that hyperinsulinemia may function as an early diagnostic indicator of the progression to diabetic conditions, obese cats have been observed to exhibit elevated plasma insulin concentrations in comparison to their ideal-weight counterparts (Appleton et al., 2000b).

Establishing precise reference ranges for hyperinsulinemia in cats remains challenging, as reported values vary considerably depending on the analytical method, physiological state, and study population (Strage et al., 2021). According to this study, baseline insulin concentrations in healthy cats ranged approximately from 2 to 18 µU/mL, depending on analytical method and physiological status (Appleton et al., 2001).

Importantly, there is no standardized threshold currently accepted for defining hyperinsulinemia in feline patients. Most authors agree that insulin values should be interpreted in light of the animal's clinical picture, including body condition, glucose levels, and insulin-to-glucose ratios, rather than relying solely on an isolated numeric cutoff.

Gene expression research on fat cats has also exposed the molecular processes underlying insulin dysregulation. Changes in the expression of genes linked to insulin signaling and glucose metabolism in both adipose and skeletal muscle tissues have been found by Stenberg et al. (2023). These results imply that alterations at the transcriptional level brought on by obesity could help explain higher insulin secretion and compromised insulin function.

3.2 Exploration of additional adipokines: resistin, chemerin, omentin, and CTRP-12

In cats, adipokines such resistin, chemerin, omentin, and CTRP-12 are crucial for controlling metabolic processes. Numerous research has examined their existence in adipose tissue and their functional relevance, providing insight into their effects on obesity and associated metabolic problems in cats.

3.2.1 Resistin

Takashima et al. molecularly cloned feline resistin and showed that it was expressed in both normal and obese cats. Resistin is known to be linked to insulin resistance in a variety of animals (Quijada et al., 2013- abstract). Although the precise routes are less known than for other species, their research showed that feline resistin levels positively linked with obesity, indicating a role in the development of insulin resistance (Takashima et al., 2016).

3.2.2 Chemerin

The involvement of another adipokine, chemerin, inflammation and metabolic control has been studied. Chemerin plays a role in immune cell recruitment and adds to the low-grade inflammation that is frequently observed in obese individuals (Recinella et al.,

2020; Sierawska and Niedźwiedzka-Rystwej, 2022; Kirichenko et al., 2022). Although the precise role of chemerin in adipose tissue in cats is still unclear, new research indicates it might be a useful indicator of metabolic disorders associated with obesity (Velde et al., 2013).

3.2.3 Omentin

Because of its insulin-sensitizing qualities, omentin may be used therapeutically to treat obesity and other metabolic diseases in cats (Appleton et al., 2000b). Omentin's anti-inflammatory properties were emphasized by Mazaki-Tovi et al., 2019a, who also discovered a negative correlation between its concentrations and body fat percentage, indicating a preventive function against the metabolic problems associated with obesity.

3.2.4 CTRP-12

Although it belongs to a family of adipokines important in metabolic control, CTRP-12 is less well-studied in cats than in humans and rodents. Although further research is required to validate these results, some research indicates that CTRP-12 may improve lipid metabolism and insulin sensitivity, which could help manage obesity in cats (Luo et al., 2023).

3.3 Adipokine dysregulation in obesity

One important element worsening a number of obesity-related illnesses in cats is adipokine dysregulation. Adipose tissue growth causes an imbalance in the secretion of several adipokines, which results in metabolic inefficiency and a persistent state of low-grade systemic inflammation. The health of cats is significantly impacted by this dysregulation, especially when it comes to developing diseases like insulin resistance, diabetes mellitus, and joint issues (Sierawska and Niedźwiedzka-Rystwej, 2022; Araújo et al., 2024; Appleton et al., 2000b).

While preventive adipokines like adiponectin are frequently decreased in obese cats, pro-inflammatory adipokines like leptin, tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) are usually secreted in greater amounts (Takashima et al., 2016; Dong et al., 2018). Despite being designed to indicate fullness and control energy balance, elevated leptin levels in obesity often result in leptin resistance, a condition in which the hypothalamus loses its sensitivity to the appetite-suppressing effects of leptin. Because too much leptin stimulates inflammatory pathways that impede the action of insulin, this phenomenon not only feeds the cycle of overeating and weight gain, but also plays a role in the development of insulin resistance (Banks and Farrell, 2003; Gerdes et al., 2011; Lynch et al., 2017; Sierawska and Niedźwiedzka-Rystwej, 2022; Kotal et al., 2023).

On the other hand, adiponectin has been linked to decreased inflammation and shows insulin-sensitizing qualities. Obese cats who have low adiponectin levels are more likely to develop metabolic diseases. An obvious illustration of how adipokine dysregulation might contribute to the development of diabetes in cats is its deficit, which has been connected to insulin resistance and

hyperglycemia (Dong et al., 2018; Sierawska and Niedźwiedzka-Rystwej, 2022; Deng and Scherer, 2010).

Nevertheless, pro-inflammatory adipokines like TNF-α and IL-6 can worsen insulin resistance and adipose tissue dysfunction, creating a vicious cycle that worsens metabolic disorders (Yu et al., 2024; Zhang, 2010). Adipokines can mediate inflammatory processes that directly affect joint health, such as osteoarthritis, which is common in obese cats and is exacerbated by persistent low-grade inflammation (Moreno-Aliaga et al., 2010).

Moreover, because obesity, inflammation and altered adipokine profiles have been related to increased cardiovascular risk, dysregulated adipokine levels can affect cardiovascular health (Lynch et al., 2017; Dadej et al., 2022; Chantemèle et al., 2011). The correlation between adipokine dysregulation and systemic health problems in cats is best illustrated by the increase in chronic illnesses linked to obesity.

3.3.1 Insulin dosing and resistance in obese cats

The intricate and multiple routes by which excess body fat causes insulin resistance and the onset of type 2 diabetes in cats represent the interactions among adipose tissue, adipokines, inflammation, and glucose metabolism. Many metabolic changes caused by increasing body fat, particularly visceral fat, promote insulin resistance, a condition defined by a reduced capacity of insulin-responsive tissues to react to the effects of insulin (Cook and Evans, 2021). Obesity is related to changes in the release of adipokines, which are signaling proteins produced by adipose

tissue. While insulin-sensitizing adipokines like adiponectin are lower, pro-inflammatory adipokines such as leptin and TNF-alpha are markedly raised in obese cats (Hoenig et al., 2013; Araújo et al., 2024). A persistent low-grade inflammatory state brought on by excessive inflammatory cytokine levels that harm insulin signaling pathways and disrupt insulin's normal metabolic functions causes increased insulin resistance and compromised glucose uptake in peripheral tissues (Zini et al., 2008). Hyperglycemia is exacerbated as a result of the liver and muscle tissues losing their sensitivity to insulin and in order to maintain normal glucose levels in the face of chronic insulin resistance, the pancreatic beta cells must produce more insulin. Insulin secretion capacities may be further compromised over time by beta-cell fatigue and malfunction brought on by the increased demand for insulin synthesis (Abdullah et al., 2010; Osto et al., 2013; Zini et al., 2008). Long-term exposure to insulin-resistant hyperglycemia in cats can cause glucotoxicity, which damages beta cells and reduces their capacity to produce insulin efficiently, the mechanism is illustrated in Figure 2 (Zini et al., 2008; Osto et al., 2013). Because of decreased glucose clearance associated with insulin resistance, postprandial glucose levels in obese cats stay noticeably higher for longer periods of time (Hoenig et al., 2011a; Appleton et al., 2000b).

These metabolic abnormalities point to a general decrease in glucose tolerance, which accelerates the development of type 2 diabetes. Inflammation connected to obesity disrupts insulin signaling and raises oxidative stress in tissues. High reactive
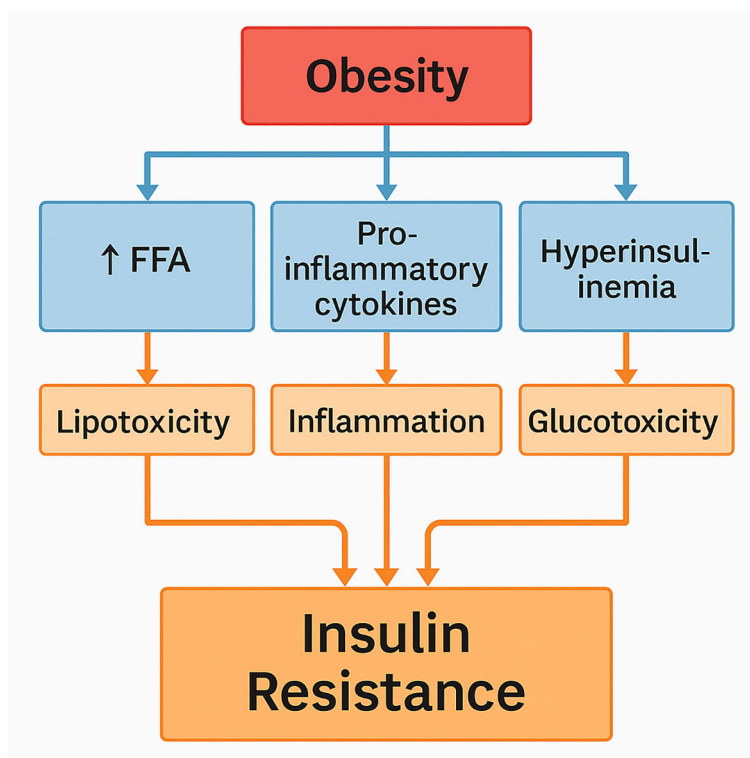

FIGURE 2
The mechanism of glucotoxicity.

oxygen species (ROS) damaging insulin signaling pathways can help to build a feedback loop maintaining metabolic inefficiency and insulin resistance (Clark and Hoenig, 2021; Zagayko et al., 2019).

The development and worsening of obesity in cats are largely caused by lifestyle factors, particularly a sedentary lifestyle and the consumption of high-calorie, nutrient-poor diets (Kocabağlı et al., 2017; Öhlund et al., 2015).

3.3.2 Species differences in adipose tissue

Dogs and cats have quite different adipose tissues in terms of composition, function, and the type of adipokines they release, which affect inflammation and metabolism. Adipocytes in dogs and cats react differently to nutritional elements and inflammatory stimuli, which can result in significant differences in the properties of their adipose tissue (Osto and Lutz, 2015).

According to research, inflammatory triggers such as lipopolysaccharides (LPS) and tumor necrosis factor-alpha (TNFα) cause adipocytes in dogs to release pro-inflammatory adipokines. For example, Ryan et al. pointed out that canine adipose cells produce inflammatory adipokines such leptin and interleukin-6 (IL-6), which may play a significant part in inflammation linked to obesity (Ryan et al., 2010). Additionally, Mazaki-Tovi et al. (2018) found that dietary fatty acids may alter the release of IL-6 and adiponectin in canine adipose tissue, suggesting that food has a direct impact on inflammatory responses and adipokine profiles. Essentially, dogs have a reactive adipose tissue phenotype, which may be a factor in disorders linked to obesity.

In contrast, the situation regarding inflammation and adipokine expression in feline adipose tissue is different. Although research shows that high-fat diets mostly increase oxidative stress rather than inflammation in their adipose depots, cats still tend to develop obesity-associated adipose tissue inflammation (Ampem et al., 2015; Osto and Lutz, 2015). Their metabolic responses may be impacted by this divergence; notable variations have been observed in the cytokine composition of adipose tissue, especially in the expression pathways that control insulin sensitivity. According to Stenberg et al., the metabolic changes in feline adipose tissue might be the result of a special evolutionary trajectory in which cats, as obligate carnivores, have different energy-storage systems than dogs (Stenberg et al., 2023).

Of their investigation of the gene expression profiles of feline adipocytes, Riedel et al. discovered unique renin-angiotensin system regulation patterns that are less noticeable in canine adipose tissues (Riedel et al., 2015). Adipokines may play different roles in regulating inflammation and energy metabolism in diverse species, as suggested by these variations. According to James et al. (2017), some adaptive responses of cats to energy mobilization and storage during times of excess or fasting have consequences for understanding how susceptible they are to metabolic diseases in comparison to dogs.

Additionally, the two species differ in the functional capacities of mesenchymal stem cells generated from adipose tissue. According to characterization studies, mesenchymal stem cells from adipose tissue in both species can differentiate into distinct lineages, but their properties and efficiency may vary depending on the tissue source. To further clarify the unique biological traits originating from their adipose tissues, Rashid et al. (2021) for instance, described the differences between the mesenchymal stem cells of dogs and cats with regard to their capacity for proliferation and differentiation (Rashid et al., 2021).

4 Potential therapeutic approaches

4.1 Dietary interventions

In both human and feline populations, dietary therapies can enhance insulin sensitivity and have a considerable impact on adipokine levels. Diets that are high in protein and low in carbohydrates have been found to have a significant impact on metabolic health, improving insulin sensitivity and altering adipokine secretion.

4.1.1 High-protein diets

Research suggests that a high-protein diet can lower pro-inflammatory adipokines like TNF-alpha and IL-6 while raising healthy adipokines like adiponectin. High-protein diets have been shown to raise serum levels of adiponectin, which have insulin-sensitizing properties, in cats (Berman et al., 2021; Öhlund et al., 2021). Adiponectin is essential for increasing insulin sensitivity because it increases muscle glucose absorption and encourages fatty acid oxidation. Diets heavy in protein have also been connected to better glycemic control since higher protein consumption raises postprandial blood glucose levels (Grant et al., 2020; Clark and Hoenig, 2021).

Although high-protein diets are often linked to concerns about renal stress, certain studies indicate they may offer advantages in particular contexts, for instance, in helping cats preserve muscle mass during the early stages of chronic kidney disease (Hall et al., 2019). These findings emphasize that the impact of dietary protein on kidney function is not uniform and must be evaluated in relation to each cat's medical profile. Notably, Kubo et al. (2023) found no harmful renal effects in healthy subjects consuming high-protein diets, suggesting that cats without kidney compromise may better tolerate elevated protein intake (Grant et al., 2020).

Given protein's fundamental role in feline health, adjusting intake based on individual health status is essential, especially in aging cats or those with existing renal issues. The interplay between protein metabolism, phosphorus levels, and kidney response reinforces the need for tailored nutritional plans that take into account each cat's unique vulnerabilities.

4.1.2 Low-carbohydrate diets

Studies show that cats' glucose metabolism may be negatively impacted by high-carb diets. According to a study, cats who consume high-carb diets nonetheless have a less ideal metabolic state even though they do not cause β-cell malfunction like some other animals do. According to Hewson-Hughes et al. (2011), a high

carbohydrate content was particularly linked to increased postprandial glucose and insulin levels, which started debates on the relevance of dietary composition in controlling cat diabetes (Verbrugghe and Hesta, 2017; Hoenig et al., 2011a; Laflamme et al., 2022).

Compared to conventional high-carb diets, low-carb diets can frequently result in more noticeable improvements in insulin sensitivity. In order to diminish insulin resistance, these diets are associated with lower serum insulin levels and less body fat accumulation. According to research, meals high in protein and low in carbohydrates may increase insulin signaling pathways, which in turn may improve glucose metabolism, better lipid profiles and a lower incidence of fatty liver disease, which is frequently a result of metabolic disturbances linked to obesity (Asaro et al., 2017; Mazaki-Tovi et al., 2013; Tricò et al., 2021; Doostvandi, 2016). These dietary changes can help in reestablishing the proper balance of adipokines by lowering pro-inflammatory cytokines and raising levels of anti-inflammatory adipokines.

High-protein, low-carbohydrate diets have been associated with improvements in insulin sensitivity and metabolic regulation in obese cats (Coradini et al., 2011). These dietary approaches influence adipokine profiles, often resulting in reduced leptin levels and increased adiponectin concentrations, thereby contributing to a lower leptin–adiponectin ratio (LAR), a marker increasingly recognized for its association with insulin resistance (Appleton et al., 2000b; Mazaki-Tovi et al., 2019a). Since a high LAR has been linked to metabolic dysfunction and inflammation, nutritional strategies that restore adipokine balance may enhance metabolic outcomes. This effect supports the potential use of LAR not only as a biomarker of metabolic status, but also as a target for monitoring response to dietary interventions (Stenberg et al., 2023).

4.2 Implications for insulin resistance in clinical practice

Cats with obesity and insulin resistance may benefit from diets high in protein and low in carbohydrates. In addition to addressing the metabolic abnormalities frequently observed in obese cats, these dietary patterns also help normalize adipokine levels and improve insulin sensitivity, which can improve general health (Mabuza et al., 2018; Clark and Hoenig, 2021).

5 Clinical implications and future direction

5.1 Clinical applications

A promising approach to treating obesity-related conditions and enhancing cats' metabolic health is to incorporate adipokine and insulin dosing techniques into veterinary practice. Veterinarians now have new therapeutic options thanks to the growing knowledge of adipokines' physiological functions and their pharmaceutical modulation. Adipokines are important for controlling insulin sensitivity, inflammation, and energy metabolism. Treating diseases like obesity and insulin resistance in cats may benefit from therapeutic modulation of these molecules. For example, dietary therapies or supplements that raise circulation levels of adiponectin may help obese cats lose weight and improve their metabolic function (Würfel et al., 2023).

In order to address obesity and related metabolic diseases, veterinarians can use dietary changes to affect adipokine levels. Low-carb, high-protein diets may improve insulin sensitivity by lowering inflammation brought on by obesity and raising adiponectin levels (Nicholson et al., 2018). Optimizing food intake and adipokine production can be achieved by creating customized nutrition programs based on each feline's unique metabolic profile (e.g. body fat percentage, body mass index, ideal body weight). Treatments aimed at increasing insulin sensitivity or weight reduction via dietary modifications, for example, might be good for cats with high leptin but low adiponectin (Mazaki-Tovi et al., 2019b).

Adipokine levels might be included in clinical practice to enhance diagnostic capabilities. Regular assessments of it can enable doctors to assess the effectiveness of weight-loss programs or treatments and modify treatment plans accordingly.

5.2 Predictive potential and clinical implications

The potential of combined hormone profiling to predict the onset of diabetes and guide early clinical interventions is substantial. The start and development of insulin resistance and type 2 diabetes mellitus have been linked to the dysregulation of major metabolic hormones, including insulin, leptin, and adiponectin, in both human and animal models. Recent human research indicates that a state of hyperinsulinemia typically precedes overt hyperglycemia, with shifts in circulating hormone levels functioning as early indicators of metabolic dysfunction (Gottlieb et al., 2022).

Increased insulin production in response to decreased insulin sensitivity in peripheral tissues is thought to cause this early hyperinsulinemia, which is further aggravated by related adipokine profile alterations. The leptin/adiponectin ratio, for instance, has been linked to a higher risk of diabetes and compromised insulin sensitivity (Gottlieb et al., 2022). Feline studies have shown similar endocrine tendencies. Studies on domestic cats has shown that there are correlations between circulating adipokine concentrations and indices of adiposity and insulin resistance (Appleton et al., 2000b). The combined use of adiponectin, leptin, and insulin profiling appears to offer a more sensitive approach for detecting subclinical metabolic disturbances, despite the fact that the majority of clinical investigations in veterinary medicine have historically relied on measuring fasting glucose or fructosamine levels. This understanding highlights the potential predictive value of combined hormone measurements in evaluating the risk of developing diabetes in obese feline patients (Appleton et al., 2000b).

Comparative research with humans and dog models—where biomarker assays are more readily available and well standardized—

further support the notion that early hormone changes are essential in the onset of metabolic disease. In spite of the promising nature of combined hormone profiling, its clinical adoption in veterinary medicine is currently limited due to several challenges. The availability and standardization of assays continue to pose significant obstacles. While human and canine studies are facilitated by well-established reference ranges and cost-effective assays, equivalent standardized methodologies for cats are still in the process of being developed (Sasaki et al., 2001). Routine clinical implementation is further complicated by the relatively high cost of sensitive multi-assays and the absence of generally recognized reference intervals for feline adiponectin, leptin, and insulin. As a result, while early hormonal changes can offer valuable insights into the progression of metabolic dysfunction, their predictive potential must be considered in the context of practical factors, including assay cost, reproducibility, and diagnostic robustness in a variety of clinical settings (Gottlieb et al., 2022; Appleton et al., 2000b).

Overcoming these analytical limitations requires targeted efforts. One key strategy is the establishment of collaborative inter-laboratory studies aimed at validating feline-specific adipokine and insulin assays. Such collaborations would allow for cross-platform comparisons, improved reproducibility, and standardization of reference ranges. Furthermore, the development and commercial availability of species-specific reagents, particularly for feline leptin and adiponectin, would enhance both clinical and research applications. Finally, harmonizing pre-analytical variables, such as fasting duration, sample type, and storage conditions should be prioritized to improve assay consistency across studies.

5.3 Current challenges and opportunities

Improving treatment strategies depends on our understanding of insulin management and adipokine regulation in feline patients. Even if literature is growing, there are still several subjects that require further study to completely grasp the underlying mechanisms of these therapies and enhance their clinical use in the management of obesity and related disorders. Despite the fact that adipokines are known to be important mediators of metabolic diseases, little is known about the precise processes by which they interact, especially when it comes to feline obesity. Adipokines including chemerin, vaspin, and visfatin require further investigation into their functions in insulin signaling pathways and inflammation (Araújo et al., 2024; Helfer and Wu, 2018).

Knowing how various adipokines interact and affect one another may help us better understand how these adipokines work together to affect insulin resistance and obesity-related health problems in cats. Most of the current research focuses on cross-sectional analyses of adipokine levels in obese versus non-obese cats, which leaves us with a limited understanding of how dietary interventions or weight loss affect adipokine profiles over time (Araújo et al., 2024; Appleton et al., 2000b). Longitudinal studies tracking adipokine levels in individual cats during the course of food changes or weight-management programs could expose

critical time periods for potential therapeutics. While studies have identified several adipokines that could help with metabolic disorders, further investigation is required to clarify their exact roles and effects in cat patients. To effectively validate adipokines and insulin as early predictive biomarkers, longitudinal studies should be designed to follow overweight but non-diabetic cats over time. A recommended model would include baseline metabolic profiling: leptin, adiponectin, insulin and glucose, followed by follow-ups every 3–6 months over a 2–3-year period. These cohorts should account for age, diet, activity level, and neuter status. Notably, biosample archiving and the inclusion of consistent assay methodologies across timepoints will be essential to allow both intra- and inter-study comparison. Such designs would help map the trajectory of metabolic deterioration and identify inflection points predictive of diabetes onset. Further study on the functions of new adipokines such CTRP12 and omentin would help to clarify, for instance, their insulin-sensitizing actions and general impact on controlling diabetes and obesity in cats (Wei et al., 2012; Elhafez et al., 2020). Targeting these adipokines pharmacologically may lead to novel therapy options.

Although dietary changes are known to influence insulin sensitivity and adipokine levels, additional controlled clinical studies are needed to exactly assess the impact of various dietary treatments on cat adipokine profiles (Araújo et al., 2024; Appleton et al., 2000b). Finding the ideal macronutrient compositions that produce the best results for metabolic health should be the main goal of future study.

Practical methods for incorporating adipokine measurements into routine veterinary practice are still unknown, despite the growing interest in using these measurements as biomarkers for conditions linked to obesity (Würfel et al., 2023; Sierawska and Niedźwiedzka-Rystwej, 2022).

6 Translational relevance and limitations

The findings presented in this paper underscore the importance of dietary strategies, metabolic pathways, and adipokine activity in both the development and management of obesity in cats. While parallels drawn from human and canine studies provide useful context and contribute to the broader understanding of these mechanisms, direct application is limited by species-specific differences, particularly in nutritional requirements, insulin responsiveness, and adipose tissue behavior. Given the unique metabolic traits of felines, clinical implementation must be approached with caution. Further cat-specific research is essential to validate these translational insights and refine therapeutic options.

7 Conclusion

In summary, this review illustrates that adiponectin, leptin, and insulin are promising early biomarkers for the prediction of

metabolic dysregulation in obese feline patients. Diminished insulin sensitivity and evident hyperglycemia have been consistently linked to decreased levels of adiponectin, elevated leptin concentrations, and compensatory hyperinsulinemia, thereby functioning as early indicators of impending diabetes mellitus. The clinical relevance of combined hormone profiling for tailored risk assessment and preventive intervention in feline practice is emphasized by the synthesis of current evidence and the parallels derived from human and canine studies. Nevertheless, there are still substantial obstacles to overcome, such as the necessity of establishing species-specific reference ranges and the development of cost-effective, standardized assays. In order to promote early therapeutic strategies and ultimately enhance clinical outcomes in obese cats, future research should concentrate on the longitudinal validation of these biomarkers, the refinement of assay methodologies, and the integration of these measures into routine preventive screening protocols.

Author contributions

LC: Writing – review & editing, Writing – original draft. SD: Conceptualization, Supervision, Writing – review & editing. AM: Methodology, Supervision, Validation, Project administration, Conceptualization, Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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