Canine diabetes mellitus risk factors: A matched case-control study

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ABSTRACT

Different subtypes of canine diabetes mellitus (CDM) have been described based on their aetiopathogenesis. Therefore, manifold risk factors may be involved in CDM development. This study aims to investigate canine diabetes mellitus risk factors. Owners of 110 diabetic dogs and 136 healthy controls matched by breed, sex, and age were interviewed concerning aspects related to diet, weight, physical activity, oral health, reproductive history, pancreatitis, and exposure to exogenous glucocorticoids. Two multivariate multivariable statistical models were created: The UMod included males and females without variables related to oestrous cycle, while the FMod included only females with all analysed variables. In the UMod, “Not exclusively commercial diet” (OR 4.86, 95%CI 2.2–10.7, P < 0.001) and “Overweight” (OR 3.51, 95%CI 1.6–7.5, P = 0.001) were statistically significant, while in the FMod, “Not exclusively commercial diet” (OR 4.14, 95%CI 1.3–12.7, P = 0.01), “Table scraps abuse” (OR 3.62, 95%CI 1.1–12.2, P = 0.03), “Overweight” (OR 3.91, 95%CI 1.2–12.6, P = 0.02), and “Dioestrus” (OR 5.53, 95%CI 1.9–16.3, P = 0.002) were statistically significant. The findings in this study support feeding not exclusively balanced commercial dog food, overweight, treats abuse, and dioestrus, as main CDM risk factors. Moreover, those results give subsidence for preventive care studies against CDM development.

1. Introduction

Different subtypes of canine diabetes mellitus (CDM) have been described based on their aetiopathogenesis (Nelson and Reusch, 2014; Gilor et al., 2016). Unlike some years ago, there is now only weak evidence supporting that most CDM cases developed immune-mediated diabetes (Ahlgren et al., 2014; Gilor et al., 2016). Nevertheless, DLA (dog leucocyte antigen) haplotypes were described with higher prevalence in predisposed breeds in comparison to less predisposed ones, and cell-mediated autoimmune destruction of beta-cells has been previously described in up to 50% of diabetic dogs (Catchpole et al., 2008). However, other causative factors have been related to CDM, such as: diseases of the exocrine pancreas, progesterone controlled GH overproduction, and secondary to hypercortisolism (Hoenig, 2002; Rand et al., 2004; Catchpole et al., 2005; Gilor et al., 2016). Despite obese dogs showing evidence of insulin resistance, beta-cell dysfunction secondary to insulin resistance seems unlikely. Moreover, no study has demonstrated how obesity can cause diabetes in dogs. Other characteristic that does not give support to a type 2 diabetes mellitus (T2DM) is pancreatic amyloidosis absence in obese diabetic dogs; however, glucotoxicity is an often-well-documented feature in CDM diagnosis (Nelson and Reusch, 2014).

Although genetic predisposition is likely important in CDM (Gilor et al., 2016), some environmental factors seem to be risk factors for diabetes development such as obesity, lack of exercise, and overfeeding (Klinkenberg et al., 2006). In this scenario, progesterone-related CDM cases are overexpressed in some regions worldwide where early elective spaying is not widespread practice. Other risk factors have been reported for both cats and humans (Rand et al., 2004; Temmeau et al., 2016; Goedecke et al., 2017). Given that CDM comprises heterogeneous disorders (Gilor et al., 2016) and is a multifactorial disease (Nelson and Reusch, 2014), this study aims to assess potential risk factors for diabetes by means of multivariable conditional logistic regression in a retrospective questionnaire based case-control study, and then, propose

Received 16 March 2017; Received in revised form 12 June 2017; Accepted 3 August 2017
2. Material and methods

2.1. Case selection process

Medical data from all CDM cases diagnosed between 2004 and 2011 were prospectively selected from a Veterinary Teaching Hospital’s Small Animal Endocrinology Service in southern Brazil. The diagnosis was based upon a fasting glycaemia > 11 mmol/L associated with glycosuria. Moreover, CDM clinical signs such as polyuria and polydipsia had to be documented. Patients with concomitant hyperadrenocorticism or hypothyroidism were not included.

2.2. Control selection process

For each diabetic dog in the study, at least one control (n:m) matched by sex, breed, and age at CDM diagnosis was randomly selected from computer files of the same general practice Veterinary Teaching Hospital. The underlying disease or reasons for the veterinary visit were not considered – only the fact that they had never been or were not diabetic.

2.3. Questionnaire

A questionnaire was previously developed, validated, and checked for accuracy in detecting owner’s perception about CDM lifespan and risk factors exposure (Pöppl et al., 2013a). While case’s variable exposure was registered prospectively during the study in standardized medical records, and questionnaire answers used for validation purposes, control owners were contacted to answer the questionnaire. To avoid recall bias, they were told that the questions considered the actual state of the dog. During prospective evaluation of cases, however, owners were asked questions regarding the dog’s lifespan before CDM initial clinical signs. The control’s questionnaires were applied over the telephone by trained interviewers and the interviews lasted 5 to 10 min, per the interviewees’ eloquence. Despite the multiple-choice design of the questionnaire, all the answers were converted to dummy (dichotomous) variables showing exposure or non-exposure to the analysed factor.

2.4. Variables under study

The “Not exclusively commercial diet” variable was classified as feeding only homemade or homemade plus commercial food. The “Frequent meals” variable was considered as feeding three or more meals a day, while the “Treats abuse” and “Table scraps abuse” variables were considered as offering pet treats or table scraps daily or many times a day. The “Inactivity” variable was classified as owner-perceived low activity. Dogs that walked more than once weekly were considered exposed to the “Outside walks” variable; whereas dogs submitted to intense physical activity at least once a week were considered exposed to the “Intense physical activity” variable. A 4 or 5 owner-perceived body condition score (BCS) on a scale from 1 to 5 was regarded as exposure to “Overweight”. The “Halitosis” and “Dental calculus” variables were classified as intense perception by the owner, while the “Tooth brushing” and “Dental prophylaxis” variables were classified, respectively, as tooth brushing at least once a month, and at least one prophylaxis under general anaesthesia in the dog’s lifetime.

The “Castration” variable was classified as gonadectomized animals, while the “ Exposure to progestogens”, “Irregular oestrous cycle” and “Dioestrus” variables were investigated only in females. Those variables were classified as: exposure to progestogens in the past 6 months, inability of the owner to predict the patient’s interoestrous interval due to unsynchronised oestrous, and heat occurrence within a period of three months, respectively. The “Pancreatitis” variable was classified as medical history of pancreatitis, while the “Glucocorticoids” variable was classified as frequent owner-related use of glucocorticoids by any route.

2.5. Statistical analysis

Since matching of cases and controls was used to control for known potential confounding variables such as sex, breed, and age, a conditional logistic regression was applied to explore the association between CDM and possible risk factors. Appropriateness of statistic methods for matched case-control studies that require specific analysis for dependent data (i.e., matched), as is the case of conditional logistic regression, was previously described (Niven et al., 2012). Odds ratio estimates and 95% confidence intervals (95% CI) were reported, and P-values less than, or equal to 0.05 were considered statistically significant.

Conditional logistic regressions for a matched case-control design were performed using the PHREG procedure in SAS. Two sets of models were developed: 1) The Unisex model (UMod), which evaluated males and females without inclusion of variables related to the oestrous cycle; 2) The Female model (FMod), which evaluated only females, including all the investigated variables. For each statistical model, a univariable analysis was initially used to explore potential risk factors for CDM. Only the variables with a P-value < 0.20 were selected for inclusion in the multivariable analysis, being subsequently screened for potential collinearity by a correlation matrix. If factors were correlated (coefficients > 0.8), the variable believed to be most related to the outcome was selected.

Conditional logistic multivariable models were built assessing all the combinations of predictors identified in the univariable analysis by adding variables recursively and selecting the best model according to Akaike Information Criterion (AIC). After that, the final model was adjusted using backward elimination to remove non-significant (P > 0.05) variables from the combination that presented the best fit according to the AIC value (i.e., the one with the lowest value). Odds ratio (OR) with a 95% confidence interval (95% CI) was estimated by the models to assess the impact of factors on the outcome. This study was approved by the Ethics Committee on Animal Use in Research of UFRGS – protocol 18336.

3. Results

3.1. Population

Of the 120 diabetic dogs diagnosed between 2004 and 2011 at Hospital’s Small Animal Endocrinology Service, 110 were initially included due to owners’ agreement with the use of their pet’s medical records. Seven owners could not be contacted at the time of CDM diagnosis and three owners refused to participate for distinct reasons. The mean age of the cases at the onset of diabetes was 10 ± 2.6 years (3 to 15 years). From a total of 143 randomly matched controls selected for the study, only seven owners refused to participate; therefore, 136 controls were eventually included after their owners’ agreement to answer the questionnaire. A total of 23 breeds were identified among diabetic cases in this study as follow: Mongrel (37); Poodle (27); Cocker Spaniel (6); Labrador Retriever (5); Pinscher and Schnauzer (4 each); Beagle, Dachshund, Fox Terrier and Maltese (3 each); Basset Hound and Siberian Husky (2 each); Akita, Bichón Frisé, Boxer, Brittany, Chow-Chow, Dalmatian, Lhasa Apso, Rottweiler, Shi Tzu, Weimaraner and Yorkshire Terrier (1 each).

3.2. Unisex model

The UMod, including all males and females without variables related to the oestrous cycle, showed statistically significant associations (P < 0.05) between CDM and risk factors in the univariable analysis (Table 1) for the following variables: “Not exclusively commercial...
diet”, “Treats abuse”, “Table scraps abuse”, and “Overweight”.

### 3.3. Female model

The FMod, which consisted of 81 female cases and 104 female controls with all the investigated variables, showed statistically significant associations ($P < 0.05$) between CDM and risk factors in the univariable analysis (Table 2) for the following variables: “Not exclusively commercial diet”, “Table scraps abuse”, “Overweight”, “Dioestrus”, “Glucocorticoids”, and “Spaying”. According to the parameter estimates of the models, the “Glucocorticoids” and “Spaying” variables were considered protective factors, while all other statistically significant variables were considered risk factors. The “Glucocorticoid” and “Pancreateatitis” variables have shown high correlation, but the “Glucocorticoid” variable was not included in the multivariate analysis based on the low biological plausibility for glucocorticoid exposure to be a protective factor against CDM. Such result is probably due to the hospital population consulted as controls. Moreover, since spaying cannot be assessed in the same model that includes the “irregular oestrous cycle” and “dioestrus” variables, it was not included in the multivariate FMod.

### 3.4. Multivariable models

Table 3 shows the OR and 95%CI end results after multivariable analysis for the UMod and FMod models.

<table>
<thead>
<tr>
<th>Variable studied</th>
<th>Cases n (%)</th>
<th>Controls n (%)</th>
<th>OR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not exclusively commercial diet</td>
<td>78 (71.0)</td>
<td>40 (29.4)</td>
<td>5.3</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Frequent meals</td>
<td>44 (40.0)</td>
<td>33 (24.3)</td>
<td>1.78</td>
<td>0.09</td>
</tr>
<tr>
<td>Treats abuse</td>
<td>47 (43.0)</td>
<td>34 (25)</td>
<td>2.12</td>
<td>0.04</td>
</tr>
<tr>
<td>Table scraps abuse</td>
<td>58 (53.0)</td>
<td>36 (26.5)</td>
<td>4.62</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Inactivity</td>
<td>42 (38.0)</td>
<td>57 (41.9)</td>
<td>0.73</td>
<td>0.36</td>
</tr>
<tr>
<td>Outside walks</td>
<td>65 (59.0)</td>
<td>74 (54.4)</td>
<td>1.38</td>
<td>0.33</td>
</tr>
<tr>
<td>Intense physical activity</td>
<td>34 (31.0)</td>
<td>62 (45.6)</td>
<td>0.73</td>
<td>0.35</td>
</tr>
<tr>
<td>Overweight</td>
<td>84 (76.0)</td>
<td>48 (35.3)</td>
<td>3.97</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Dental calculus</td>
<td>23 (21.0)</td>
<td>24 (17.6)</td>
<td>1.79</td>
<td>0.2</td>
</tr>
<tr>
<td>Halitosis</td>
<td>21 (19.0)</td>
<td>14 (10.3)</td>
<td>1.84</td>
<td>0.27</td>
</tr>
<tr>
<td>Toothbrushing</td>
<td>14 (13.0)</td>
<td>36 (26.5)</td>
<td>0.5</td>
<td>0.12</td>
</tr>
<tr>
<td>Dental prophylaxis</td>
<td>33 (30.0)</td>
<td>41 (30.1)</td>
<td>0.94</td>
<td>0.87</td>
</tr>
<tr>
<td>Pancreateatitis</td>
<td>20 (18.0)</td>
<td>6 (4.4)</td>
<td>2.68</td>
<td>0.11</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>6 (7.0)</td>
<td>18 (13.2)</td>
<td>0.42</td>
<td>0.18</td>
</tr>
<tr>
<td>Castration</td>
<td>44 (40.0)</td>
<td>70 (51.5)</td>
<td>0.54</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Table 3 Results of multivariable conditional logistical regression analysis for both unisex model (UMod) and female model (FMod) expressed in odds ratio (OR) with 95% confidence interval (95% CI).

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UMod</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not exclusively commercial diet</td>
<td>4.86</td>
<td>2.2-10.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Overweight</td>
<td>3.51</td>
<td>1.6-7.5</td>
<td>0.001</td>
</tr>
<tr>
<td>FMod</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dioestrus</td>
<td>5.53</td>
<td>1.9-16.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Not exclusively commercial diet</td>
<td>4.14</td>
<td>1.3-12.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Overweight</td>
<td>3.91</td>
<td>1.2-12.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Table scraps abuse</td>
<td>3.62</td>
<td>1.1-12.2</td>
<td>0.03</td>
</tr>
</tbody>
</table>

4. Discussion

The main finding of this study is that cases were more exposed to studied risk factors such as not exclusively commercial diet and overweight than the matched nondiabetic controls. These findings remain statistically significant even after the multivariable regression model. Furthermore, potentially different subtypes of CDM were included in the case series. When the multivariable model was applied to females, the fact that diabetic females were more exposed to dioestrus at diagnosis came as no surprise as progesterone-related diabetes mellitus is a common type of CDM in our setting (Pöppl et al., 2013a,b). In the FMod model, though, the higher exposure of cases to treats abuse, overweight, and not exclusively commercial diet is in line with the results obtained by Wejdmark et al. (2011).

The exclusion of cases with hyperadrenocorticism or hypothyroidism, as well as the matching of controls by breed, sex and age, allowed elimination of possible biases associated with these factors, given that breed, advanced age, female sex, and other endocrine diseases have all been previously described as risk factors for CDM (Peterson et al., 1984; Guptill et al., 2003; Fall et al., 2007; Fukuta et al., 2012). The breedes most frequently identified in this study are popular in our region and prone to the development of diabetes, especially Poodles, although the prevalence rates of canine diabetes in different regions is affected by fads and local preferences (Hess et al., 2000; Hoening, 2002; Guptill et al., 2003; Fracassi et al., 2004; Catchpole et al., 2005; Fall et al., 2007). Misclassification bias was probably not present in the present study since diabetes is easy to recognize and the diagnostic criteria adopted was clear.

For both models, after the multivariable analysis, the chances of CDM among dogs receiving not exclusively commercial diet in the life history was at least four times the chance of CDM among the dogs receiving commercial diet exclusively. Feeding the dog a commercially available diet + homemade food, or exclusively homemade food, is often associated with a high-calorie diet with high carbohydrate and high fat content (Bland et al., 2009), predisposing to obesity (German, 2006). Exposure to high-fat diet was associated with lower glucose tolerance secondary to reduction in the beta-pancreatic cell activity (Kaiyala et al., 1999), as well as with larger appetite due to the lower insulin transport to the central nervous system (Kaiyala et al., 2000), which highlights high-calorie diets as a risk factor for obesity and diabetes. Likewise, activation of molecular pathways associated with insulin resistance in T2DM has been attributed to overfeeding and overweight (Saltiel and Kahn, 2001; Ozcan et al., 2004). Investigating homemade food's ingredients and proportion of homemade and commercial diets, when this was the case, is beyond the scope of this study; however, all owners denied that their dogs' feeding regime with not exclusively commercial foods was elaborated by a veterinary nutrionist. This fact enhances the probability of those diets being in fact unbalanced, carbohydrate and fat-rich diets.
Vet treats or table scraps abuse are predisposing factors for weight gain (German, 2006; Sallander et al., 2001; Bland et al., 2009; German et al., 2011; Heuberger and Wakshlag, 2011), being also implicated as risk factors for the development of diabetes (Klinkenberg et al., 2006). Nevertheless, when we conducted a correlation matrix analysis among those variables, there was no high correlation, and thus they were assumed to be independent variables. Only the frequency at which treats were given to the animals was accounted for, but not their amount. This factor was statistically significant in the FMod, but not in the UMod after the multivariable analysis. This may have occurred due to the inclusion of oestrous cycle variables.

In any case, the fact that the chance of CDM among bitches exposed to table scraps abuse was 3.62 times the chance of CDM among female not exposed to table scraps abuse are in consonance with exposure to a not exclusively commercial diet and predisposition to obesity (Heuberger and Wakshlag, 2011). The Kappa score (sensitivity of 91.5%, $P < 0.001$) for this variable in the questionnaire was 0.91 (Pöppl et al., 2013a) which was considered excellent, even though this information might not be entirely accurate. Owners probably tend to downplay their possible role in the disease development, understating the number of treats given, or conversely, overstating it trying to explain the development of their dog’s disease (Wejdmark et al., 2011). Recall and confounding biases were possible limitations in this study. Diabetic status causes emaciation and many patients at diagnosis were no longer overweight (Nelson, 2015). In addition, dog owners have difficulty assessing the body condition of their pets, especially when they are overweight (Heuberger and Wakshlag, 2011; White et al., 2011). Moreover, the inclusion of hospital controls, may have underestimated control group’s obesity prevalence since this could include animals that failed to gain weight, or that have diseases leading to low body condition score.

Although obesity is a key factor involved in the pathogenesis of T2DM in humans and in felines, no study has demonstrated how it can cause diabetes in dogs (Rand et al., 2004; Gilor et al., 2016). Canine obesity is associated with several factors such as genetics, reproductive management, and nutritional and physical management through the positive balance between calorie intake and energy expenditure (German, 2006; Bland et al., 2009). The association between overweight and obesity in adult life and the development of diabetes has been documented in dogs for over 50 years (Krook et al., 1960; Mattheeuws et al., 1984; Klinkenberg et al., 2006; Wejdmark et al., 2011).

Studies have shown over the years that obese dogs have insulin resistance associated with a lower beta cell response, leading to lower glucose tolerance (Mattheeuws et al., 1984; Rand et al., 2004; German et al., 2009). Besides, the higher secretion of inflammatory adipokines by adipocytes in response to overweight, justifies insulin resistance in obesity (Saltiel and Kahn, 2001; German et al., 2009; Kil and Swanson, 2010). Nevertheless, reduced concentrations of adiponectin are not seen in all overweight dogs, and this may help prevent beta cell loss. Furthermore, increased leptin levels in obese dogs help beta-cells compensate for insulin resistance (Verkest et al., 2011a,b). If the beta-cells of dogs exposed to insulin resistance do not improve their insulin secretion ability properly, hyperglycaemia and beta cell depletion (glucotoxicity) may develop (Imamura et al., 1988; Wejdmark et al., 2011; Mared et al., 2012). This is similar to what is observed in the transition from non-insulin dependent diabetes to insulin-dependent diabetes in humans. Moreover, dog’s pre-diabetes is poorly characterized (Gilor et al., 2016). Obese dogs have greater post-prandial glucose and triglycerides levels (Verkest et al., 2012). Nevertheless, the latter authors conclude that canine beta-cells are either not sensitive to toxicity because of mild hyperglycaemia, or lack another component of the pathophysiology of beta cell failure in T2DM because fasting insulin sensitivity was five times lower in obese dogs than in lean ones, whereas fasting beta cell function was 2.5 greater in obese animals than in lean ones. In contrast, when a dog becomes clinically diabetic, it is completely dependent on exogenous insulin to survive due to hypoinsulinemia (Nelson, 2015). Despite this data, beta-cells glucotoxicity induced by obesity were never demonstrated in dogs.

The high odds ratio found for dioestrus in the FMod is in line with previous studies which demonstrated insulin resistance during dioestrus (Eingenmann et al., 1983; Selman et al., 1994; Scaramal et al., 1997; Fukuta et al., 2012; Mared et al., 2012) or higher incidence of diabetes during this phase of the oestrous cycle (Fall et al., 2010; Pöppl et al., 2013a,b).

The higher incidence of diabetes in females only occurs where elective spaying is not a widespread practice (Catchpole et al., 2005) due to the eminent production of growth hormone (GH) by the mammary gland in response to endogenous or exogenous progestogens (Eingenmann et al., 1983; Selman et al., 1994). In addition to the influence of progesterone on the insulin binding characteristics to its receptor (Ryan and Enns, 1988; Pöppl et al., 2016) and to the reduced phosphorylation of insulin receptor in response to progesterone (Pöppl et al., 2012), GH causes insulin resistance through multiple mechanisms in the crosstalk between the intracellular communication pathways of GH and of insulin signalling (Dominici et al., 2005).

Some limitations of this study should be pointed out. The fact that our results are questionnaire based, despite previous questionnaire validation, may have brought bias. For example, owners of diabetic dogs may be more prone to remember details of dog’s lifespan regarding feeding, previous diseases, oestrus cycle, and medical history than owners of controls, i.e. recall bias. Moreover, hospital controls employment, even though they were not diabetic, may also have become a bias source as well. However, this approach helps us select patients from the same population, a crucial case-control studies rule. General owner’s inability to accurately give information about health status of their dogs may have affected our results; however, we assume that this ability is similar for both case and control owners. Misclassification bias is less likely in our study. Clinical CDM is easy to recognize by owners and it is unlikely that any control was diabetic at the time of the questionnaire, despite some controls possibly being reclassified as cases in later years. Most of those limitations would be reduced or nullified if a cohort study was designed instead of a case-control one. However, cohort studies are longer and harder due to selection of cases and controls from exposure status and then followed longitudinally (Wejdmark et al., 2011).

Even though many forms of diabetes are probably represented in this study with several breeds, the risk factors associated with CDM were like those reported by other authors (Klinkenberg et al., 2006; Wejdmark et al., 2011), and it is possible that these environmental influences are present worldwide, helping explain the greater incidence of CDM over the past decades (Guptill et al., 2003). Based on this, and on extant evidence, this paper argues that feeding dogs exclusively balanced commercial dog food, keeping an ideal BCS, avoiding treats abuse, and females early spaying, may be protective factors against CDM development. However, the impact of those potential protective factors should be further studied as preventive procedures against CDM development. Furthermore, future research on mechanisms by which overfeeding and overweight may lead to CDM are needed.

**Funding**

This study was funded by CNPq (Brazilian National Research Council).

**Conflict of interest**

None.

**Acknowledgements**

We would like to thank the > 200 dog owners who kindly helped us.
by agreeing to answer the questionnaire, and the entire staff of the Medical and Statistical Archives Sector of the Hospital. We are thankful to DVM Leticia Machado and DVM Luciana de Jesus for their contribution while preparing this manuscript.

References


