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Prevalence, Clinical Picture, and Risk Factors Associated with Diabetes Mellitus in Dogs in Alexandria Governorate, Egypt

Meray Mikhaiel, Mohamed Nasr, Nabil Bakeer, Noha Beder, Besheer Elshafey and Asmaa Saleh

Department of Animal Medicine, Faculty of Veterinary Medicine, Damanhour University, Damanhour, Egypt

Abstract

This study was conducted to determine the prevalence, clinical picture, complications, and risk factors associated with Diabetes Mellitus in dogs in Alexandria governorate, Egypt. One hundred and thirty-nine dogs representing fifteen breeds from the Directorate of Veterinary Medicine in Alexandria governorate were involved in the study between November 2020 and April 2021. After a thorough clinical examination and filling out a pre-designed questionnaire, random blood glucose (RBG) test was performed for all animals. Those with high RBG levels were subjected to a complete blood picture (CBC), liver and kidney functions, and HbA1c. A control group of 50 dogs of similar age, sex, breed, and management was selected and subjected to the same analyses. The prevalence of DM among the studied dogs was 7.2 %. All diabetics suffered from polydipsia and polyuria, while 60% suffered from polyphagia and 80% suffered from weight loss. No significant impact of DM on temperature, respiratory rate, anaemia, liver enzymes and platelets count, but there was a significant increase in pulse rate. There was a significant impact of DM on eyes as 80% of the diabetic dogs suffered from cataracts. It had a significant impact on total leucocyte count and on the renal function, where 70 % of the diabetics had impaired renal functions. Regarding the risk factor analysis associated with the occurrence of DM, only breed has been identified as a potential risk factor for cDM (canine diabetes mellitus). So, a spotlight must be thrown on cDM as an essential and not uncommon dog's disease, and we need to raise awareness of cDM among veterinarians and dogs' owners.

Keywords: Diabetes Mellitus; Clinical picture; Risk factors; Dogs

*Correspondence: Asmaa Saleh
Department of Animal Medicine, Faculty of Veterinary Medicine, Damanhur University, Damanhur, Egypt
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1. Introduction

Diabetes mellitus (DM) is one of the most prominent and common metabolic disorders that have been described in dogs **(Nelson and Reusch, 2014).** It is caused by an absolute or a relative insulin deficiency **(Shopback and Gardner, 2011).** And because of the insufficiency of insulin, an abnormal high glucose level was detected in the bloodstream, as insulin is essential to transport glucose from the plasma to the cells **(Robinson et al. 2016; Miller and Brines, 2018).** There are potential multifactorial factors involved in the etiology and pathogenesis of canine diabetes mellitus in dogs. It could be summarized in; Genetic predispositions, immune-mediated insulitis, pancreatitis, some infections, diabetogenic drugs and toxic chemicals, concurrent hormonal disease including hyperthyroidism, hyperadrenocorticism, diestrus-induced excess growth hormone, glucocorticoids, progestogens, concurrent kidney, and cardiac illness **(Guptill et al. 2003; Feldman and Nelson, 2004; Nelson and Reusch, 2014).** The most common clinically recognized form of diabetes mellitus in dogs resembles type 1 diabetes mellitus in humans **(Montgomery et al. 1996).** Classical clinical signs of diabetes include weight loss, polyphagia, polydipsia, and polyuria with ketonuria and ketoacidosis as a complication **(Santaguida et al. 2005, Nelson and Reusch, 2014).** This study was conducted to determine the prevalence, clinical picture, complications, and risk factors associated with Diabetes Mellitus in dogs in Alexandria governorate, Egypt.

2. Materials and Methods

2.1. Animals and experimental design

One hundred and thirty nine dogs representing fifteen breeds (44 German Shepherds, 25 Golden Retrievers, 26 Toy dogs, 9 Rottweilers, 8 Pitbulls, 7 Huskies, 6 Cane Corsos, 5 Great Danes, 2 Caucasian Shepherds, 2 Mastiffs, 1 Doberman, 1 Labrador Retriever, 1 Dutch Shepherd, 1 Saint Bernard, and 1 Balady) aged from 2.5 to 144 months (29.53 ± 28.52) and weighing from 2-80 Kg (31.54 ± 18.58), were admitted to Directorate of Veterinary Medicine in Alexandria governorate between November 2020 and April 2021 and were chosen for the study.

The ethical committee of the Faculty of Veterinary Medicine, Damanhour University (DMU-VET-IMED-2022-01) approved the research protocol. All animal handling and procedures were carried out following national animal care and welfare.

After a thorough clinical examination and filling out a pre-designed questionnaire, Random Blood Glucose (RBG) test was performed for all animals using a blood glucose analyzer, Rightest GM300 **(Bionime GmbH, Switzerland)**. Those with high RBG levels (≥110mg/dl) were subjected to the following analyses: complete blood picture (CBC), liver function, kidney function, and HbA1c. Dogs that had HbA1c ≥6.5 % were considered diabetics. Control group of fifty dogs of similar age, sex, breed, and management was selected and subjected to the same analyses. The full description for experimental design and samples enrolled in study were explained in **Figure 1**.

2.2. Questionnaire

All enrolled dogs' owners were interviewed and asked to complete a pre-designed questionnaire of dog data as gender, age and breed, diet and management, vaccination and if they are suffering from any symptoms of DM (polydipsia, polyurea, polyphagia, weight loss, recurrent infections according to **(Petrie, 1996)**.

2.3. Clinical examination

All animals were subjected to thorough clinical examination, including body weight, temperature, pulse and respiratory rates, inspection, palpation, percussion, and auscultation for different systems in addition to eye and skin examination **(Hardy, 1981).**

2.4. Samples collection and processing

Two blood samples (with and without EDTA) were collected in clean and dry tubes by puncturing the cephalic vein using needles (gauge 22) from 32 dogs with high RBG (≥ 110 mg/dl) and the control group of RBG (<110mg/dl) according to **(McGuill and Rowan, 1989; Morton, 1993; Diehl et al., 2001; Hoggatt et al., 2016).** The blood with EDTA was collected in a clean and dry tube and used to perform CBC and glycosylated hemoglobin (HbA1c). The blood without EDTA was used for serum separation and biochemical analysis of aspartate transaminase (AST), alanine transaminase (ALT), urea and creatinine.

2.5. HbA1c analysis

The RBG test was positive in 32 139 dogs (≥ 110mg/dl). Only ten of the thirty-two dogs tested were positive for HbA1c (≥ 6.5%) and were defined as a diabetic group according to **(Lane and Cooper, 1994; Wills and Simpson, 1994; Rucinsky et al., 2010; Goemans et al., 2017)**. HbA1c analysis is performed using a specific protein analyzer for HbA1c; MISPA-i2 **(Agappe Co., Switzerland).**

2.6. Hematological analysis

CBC was performed for all positively random blood glucose (32 dogs) and animals of the control group using Automated CBC 3 parts differential apparatus; ABX Micros ES60 **(Horiba Medical Co., France)** according to **(Jain, 2000).**

2.7. Liver and kidneys functions tests

All positively random blood glucose (32 dogs) and animals of the control group were subjected to analysis of; blood urea nitrogen and creatinine using Colorimetric kits for detection of urea and creatinine (**Diasys-Co., Germany)** according to **(Patton and Crouch, 1977)**, serum AST and ALT activities using colorimetric kits for detection of ALT and AST **(Diasys-Co., Germany)** according to **(Reitman and Frankel, 1957)** were performed using Semi-automated photometer **(Diasys-Co., Germany).**

2.8. Statistical analysis

Data were collected, revised, coded, and fed to the statistical software SPSS version. The following statistical tests were used:

1. Descriptive statistics: The means with standard deviation and percent were used to describe the scale and categorical data, respectively.
2. Numeric data:
   a. Kolmogorov-Smirnov was used for testing the normal distribution of the current data.
   b. ANOVA and Kruskal Wallis test were used to compare means of different parameters among the groups.
3. Analysis of categorical data:
   a. Pearson's Chi square test was used to reflect a real association between Diabetes mellitus (DM) and different variables of clinical findings.
   b. Monte Carlo exact test (MC) and Fishers exact test were used when there were many small, expected values.
4. Logistic regressions test: Analysis of risk factors potentially associated with the occurrence of DM was evaluated in two steps using logistic regression. In the first step, we conducted a univariate analysis of each hypothesized risk factor (independent variables) and selected those variables with $p \leq 0.2$ for further multivariable logistic regression analysis.

3. Results

The result of the present work will be displayed under 3 sections:

I- Distribution of dogs under study according to RBG and HbA1c.

II-Case control study for those having high RBG level and a control group to detect the impact of Diabetes Mellitus (DM) and high RBG level on different items.

III-Risk assessment study for DM in dogs under investigation.

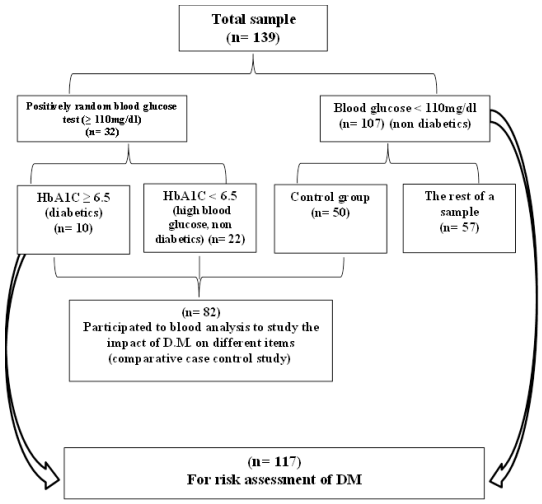

Figure 1. Flow chart explaining the sample enrolled in the study

3.1. Distribution of the dogs under study according to RBG and HbA1c

In our study, 32 dogs out of 139 (23%) had RBG ≥ 110 mg/dl. Ten dogs (7.2 %) had HbA1c (≥ 6.5 %) with RBG≥ 200 mg/dh (**Table 1**).

3.2. Impact of DM and high RBG level on different parameters in dogs (total number 82 dogs):

3.2. a. Clinical findings

It was found that there was no significant impact of DM on recurrent infections, while DM was significantly associated with weight loss ($p < 0.001$) where 80% of diabetic animals were underweight compared to 13.6% and 16% in high RBG and the control group, respectively **(Table 2** and **Figure 2)**. A significant association ($p < 0.001$) between DM and increased appetite, polydipsia and polyuria in diabetic dogs were found **(Table 2)**. When comparing diabetics to those with normal blood glucose levels, there was no significant difference in temperature or respiratory rate, but there was a significant increase ($p = 0.003$) in pulse rate **(Table 3)**. There was a significant impact of DM on the eyes of diseased dogs. 80% of the diabetics suffered from cataracts compared with 31.8% of those with high RBG levels and 16.0% of the control group **(Table 4** and **Figure 3)**.

3.2. b. Blood picture

Although DM led to decreased Hb in large numbers of diabetic animals (70%), this decrease was not significant. DM had a significant impact on total leucocyte count ($p < 0.001$). However, platelet count had no significant impact **(Table 5).**

3.2. c. Liver and kidneys functions tests

There was no significant impact of DM on liver enzymes, where the mean values of AST & ALT in diabetics were 45.97 ± 32.84 and 63.40 ± 76.09, respectively vs 33.35 ± 16.30 and 34.85 ± 28.97 in the control group **(Table 6)** while. There was a significant impact of DM on the renal function, where 70 % of the diabetics had impaired renal functions compared with 0% of the control group. The median value of urea significantly increased 64.5 (50.0-74.0) ($p < 0.001$) in DM group compared with 39.50 (35.0 – 51.0) and 36.50 (26.0 – 48.0) in high RBG and control groups, respectively. The median of creatinine among DM group was 1.30 (1.2 – 1.7) compared with 0.90 (0.80 – 1.1) and 0.90 (0.90 – 1.1) in high RBG and control groups, respectively **(Table 7)**.

3.3. Risk assessment study for DM in dogs

Regarding the risk factor analysis associated with the occurrence of DM, only breed and age were significant in the univariate analyses ($p \leq 0.2$) and subjected to multivariate logistic regression analyses. The only breed has been identified as a potential risk factor for DM in dog. Forty percent of pitbull dogs were diabetics. They were at high risk and recorded 35 times more chance of having diabetes than other breeds ($p < 0.015$; OR: 35.04; CI 95 % 1.997-615.0). **(Tables 8a** and **8b)**.

Table 1. Distribution of dogs under study according to RBG and HbA1c

	Total (n = 139)		**RBG ≥110 (n = 32)**		**RBG ≥110 & HBA1c ≥6.5 (n = 10)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
RBG (mg/dl)						
<110	107	77.0	0	0.0	0	0.0
110 – <200	22	15.8	22	68.8	0	0.0
≥200	10	7.2	10	31.3	10	100.0
Min. – Max.	46.0 – 411.0		110.0 – 411.0		206.0 – 411.0	
Mean ± SD.	103.18 ± 44.64		155.88 ± 67.61		241.20 ± 61.76	
HbA1c (%)						
NA	57	41.0	0	0.0	0	0.0
<6.5	72	51.8	22	68.7	0	0.0
≥6.5	10	7.2	10	31.3	10	100.0
n	**82 (50+32)**		**32**		**10**	
Min. – Max.	2.90 – 13.30		2.90 – 13.30		6.60 – 13.30	
Mean ± SD.	3.72 ± 1.94		5.01 ± 2.64		8.20 ± 2.09	

RBG: random blood glucose **HbA1c:** glycosylated hemoglobin **SD:** standard deviation

Table 2. Impact of D.M. and high blood glucose on some clinical findings in dogs

	RBG ≥110 & HBA1c ≥6.5 (n = 10)		**RBG ≥110 & HbA1c <6.5 (n = 22)**		**Control (RBG <110) (n = 50)**		χ^2	^{MC}p
	No.	**%**	**No.**	**%**	**No.**	**%**		
Recurrent infection								
No	8	80.0	21	95.5	49	98.0	4.696	0.052
Yes	2	20.0	1	4.5	1	2.0		
Weight loss								
No	2	20%	19	86.4	42	84	20.709*	<0.001*
Yes	8	80%	3	13.6	8	16		
Appetite								
Normal	5	50.0	17	77.3	47	94.0	17.608*	<0.001*
Increase appetite	4	40.0	1	4.5	0	0.0		
Decrease appetite	1	10.0	4	18.2	3	6.0		
Polydipsia								
No	0	0.0	21	95.5	50	100	50.089*	<0.001*
Yes	10	100	1	4.5	0	0.0		
Urination								
Normal	1	10.0	18	81.8	47	94.0	41.408*	<0.001*
Polyuria	9	90.0	3	13.6	0	0.0		
Oliguria	0	0.0	1	4.5	1	2.0		
Dysurea	0	0.0	0	0.0	2	4.0		

χ^2: **Chi square test** MC: **Monte Carlo**
p: p value for comparing between the studied groups *: Statistically significant at $p \leq 0.05$

Table 3. Impact of D.M. and high blood glucose on body temperature, pulse, and respiratory rates

parameters	**RBG ≥110 & HBA1c ≥6.5 (n = 10)**		**RBG ≥110 & HBA1c <6.5 (n = 22)**		**Control (RBG <110) (n = 50)**		**Test of sig.**	**p**
	No.	**%**	**No.**	**%**	**No.**	**%**		
Temperature (°C)								
Normal (38-39.5°C)	8	80.0	22	100.0	49	98.0	χ^2= 5.462	^{MC}p= 0.052
Increase	2	20.0	0	0.0	1	2.0		
Min. – Max.	38.0 – 41.0		38.0 – 39.10		38.0 – 40.0		F= 2.895	0.061
Mean ± SD.	39.11 ± 0.86		38.66 ± 0.40		38.75 ± 0.44			
Pulse rate/min								
Normal	6	60.0	19	86.4	49	98.0	χ^2= 11.681*	0.002*
Increase	4	40.0	3	13.6	1	2.0		
Min. – Max.	98.0 – 133.0		82.0 – 130.0		80.0 – 130.0		F= 6.453*	0.003*
Mean ± SD.	110.5 ± 9.74		97.23 ± 11.56		97.04 ± 11.06			
Sig. bet. grps.	p_1=0.007*, p_2=0.002*,p_3=0.998							
Respiratory rate (breaths/min)								
Normal	6	60.0	18	81.8	45	90.0	χ^2= 5.295	^{MC}p= 0.060
Increase	4	40.0	4	18.2	5	10.0		
Min. – Max.	13.0 – 33.0		10.0 – 33.0		12.0 – 58.0		F= 0.916	0.404
Mean ± SD.	22.70 ± 7.72		19.32 ± 5.98		21.60 ± 8.29			

SD: **Standard deviation** χ^2: **Chi square test**
F: **F for ANOVA test**, pairwise comparison bet. each 2 groups was done using **Post Hoc Test, (Tukey)** MC: **Monte Carlo**
p: p value for comparing between the studied groups
p_1: p value for comparing between **RBG ≥110 & HBA1c ≥6.5 and RBG ≥110 & HBA1c <6.5**
p_2: p value for comparing between **RBG ≥110 & HBA1c ≥6.5 and control (RBG<110)**
p_3: p value for comparing between **RBG ≥110 & HBA1c <6.5and control (RBG<110)**
*: Statistically significant at $p \leq 0.05$

Table 4. Impact of D.M. and high RBG on eye

Eye examination	RBG ≥110 & HBA1c ≥6.5 (n = 10)		RBG ≥110 & HBA1c <6.5 (n = 22)		Control (RBG <110) (n = 50)		χ^2	^{MC}p
	No.	%	No.	%	No.	%		
Normal	2	20.0	15	68.2	42	84.0	18.396*	<0.001*
Cataract	8	80.0	7	31.8	8	16.0		
Congested sclera	0	0.0	0	0.0	0	0.0		
pale mucosa	0	0.0	0	0.0	0	0.0		

χ^2: **Chi square test** MC: **Monte Carlo p**: p value for comparing between the studied groups
*: Statistically significant at $p \leq 0.05$

Figure 2. Diabetic German Shepherds suffering from weight loss

Figure 3. Toy and Pitbull diabetic dogs suffering from cataract

Table 5. Impact of DM and high RBG level on blood picture

Blood picture	RBG ≥110 & HBA1c ≥6.5 (n = 10)		RBG ≥110 & HBA1c <6.5 (n = 22)		Control (RBG <110) (n = 50)		Test of sig.	p
	No.	%	No.	%	No.	%		
Hemoglobin(g/dl)							χ^2=	
Normal (12.5-<16)	2	20.0	7	31.8	31	62.0	12.584*	^{MC}p=
Increase	1	10.0	2	9.1	0	0.0		0.006*
Decrease	7	70.0	13	59.1	19	38.0		
Min. – Max.	5.20 – 17.90		5.0 – 16.30		8.90 – 15.10		F=	0.155
Mean ± SD.	11.67 ± 3.58		11.72 ± 2.72		12.65 ± 1.37		1.911	
TLC ($\times 10^3/cm^3$)								
Normal (4-11)	3	30.0	6	27.3	36	72.0	χ^2=	^{MC}p
>11.0 – 13.0	3	30.0	6	27.3	10	20.0	23.981	<0.001*
>13.0 – 15.0	1	10.0	5	22.7	4	8.0		
>15.0	3	30.0	5	22.7	0	0.0		
Min. – Max.	4.30 – 47.40		4.80 – 17.70		4.10 – 14.10		H=	<0.001*
Mean ± SD.	15.73 ± 12.04		12.69 ± 2.90		9.41 ± 2.53		19.501*	
Median (IQR)	12.35(10.7 – 17.1)		12.80(11.0 – 14.5)		9.25(7.5 – 12.0)			
Sig. bet. grps.	p_1=0.649, p_2=0.012*, p_3<0.001*							
Platelets								
Normal (150000-450000)	9	90.0	18	81.8	49	98.0	χ^2=	0.066
Increased	0	0.0	2	9.1	0	0.0	7.426	
Decreased	1	10.0	2	9.1	1	2.0		

SD: **Standard deviation** IQR: **Inter quartile range**
χ^2: **Chi square test** MC: **Monte Carlo**
H: H for **Kruskal Wallis test,** pairwise comparison bet. each 2 groups were done using **Post Hoc Test (Dunn's for multiple comparisons test)**
p: p value for comparing between the studied groups
p_1: p value for comparing between **RBG ≥110 & HBA1c ≥6.5 and RBG ≥110 & HBA1c <6.5**
p_2: p value for comparing between **RBG ≥110 & HBA1c ≥6.5 and control (RBG<110)**
p_3: p value for comparing between **RBG ≥110 & HBA1c <6.5and control (RBG<110)**
*: Statistically significant at $p \leq 0.05$

Table 6. Impact of DM and high RBG level on liver function

Liver function	RBG ≥110 & HBA1c ≥6.5 (n = 10)		RBG ≥110 & HBA1c <6.5 (n = 22)		Control (RBG <110) (n = 50)		Test of sig.	p
	No.	%	No.	%	No.	%		
AST (U/L)								
Normal (16-60)	9	90.0	22	100.0	50	100.0	$\chi2$= 4.472	^{MC}p= 0.126
Increase	1	10.0	0	0.0	0	0.0		
Min. – Max.	12.0 – 130.0		16.0 – 58.0		11.0 – 56.0		H= 2.856	0.240
Mean ± SD.	45.97 ± 32.84		32.09 ± 11.11		31.38 ± 12.29			
Median (IQR)	34.50(30.0 – 56.7)		29.0(23.0 – 41.0)		28.50(22.0 – 39.0)			
ALT (U/L)								
Normal (18-86)	9	90.0	22	100.0	50	100.0	$\chi2$= 4.472	^{MC}p= 0.126
Increase	1	10.0	0	0.0	0	0.0		
Min. – Max.	22.0 – 274.0		20.0 – 49.0		16.0 – 51.0		H= 2.900	0.235
Mean ± SD.	63.40 ± 76.09		30.77 ± 6.84		30.94 ± 10.71			
Median (IQR)	35.0(24.0 – 65.0)		31.0(27.0 – 34.0)		29.50(21.0 – 36.0)			

SD: **Standard deviation** IQR: **Inter quartile range** H: H for **Kruskal Wallis test**
χ^2: **Chi square test** MC: **Monte Carlo**
p: p value for comparing between the studied groups

Table 7. Impact of D.M. and high blood glucose on renal function

Renal function	RBG ≥110 & HBA1c ≥6.5 (n = 10)		RBG ≥110 & HBA1c <6.5 (n = 22)		Control (RBG <110) (n = 50)		Test of sig.	p
	No.	%	No.	%	No.	%		
Urea (mg/dl)								
Normal (10-60)	3	30.0	21	95.5	50	100.0	$\chi2$= 29.122*	<0.001*
Increase	7	70.0	1	4.5	0	0.0		
Min. – Max.	50.0 – 120.0		17.0 – 70.0		19.0 – 59.0		H= 20.971*	<0.001*
Mean ± SD.	69.01 ± 21.74		42.45 ± 13.94		37.20 ± 11.50			
Median (IQR)	64.50(50.0 – 74.0)		39.50(35.0 – 51.0)		36.50(26.0 – 48.0)			
Sig. bet. grps.	p_1=0.002*,p_2<0.001*,p_3=0.132							
Creatinine (mg/dl)								
Normal (up to 1.2)	3	30.0	22	100.0	50	100.0	$\chi2$= 31.068*	<0.001*
Increase	7	70.0	0	0.0	0	0.0		
Min. – Max.	0.50 – 3.10		0.50 – 1.20		0.60 – 1.20		H= 14.522*	0.001*
Mean ± SD.	1.48 ± 0.70		0.92 ± 0.19		0.94 ± 0.15			
Median (IQR)	1.30(1.2 – 1.7)		0.90(0.80 – 1.1)		0.90(0.90 – 1.1)			
Sig. bet. grps.	p_1<0.001*,p_2<0.001*,p_3=0.672							

SD: **Standard deviation** QR: **Inter quartile range** *: Statistically significant at $p \leq 0.05$
H: H for **Kruskal Wallis test,** Pairwise comparison bet. each 2 groups was done using **Post Hoc Test (Dunn's for multiple comparisons test)** p: p value for comparing between the studied groups
p_1: p value for comparing between **RBG ≥110 & HBA1c ≥6.5 and RBG ≥110 & HBA1c <6.5**
p_2: p value for comparing between **RBG ≥110 & HBA1c ≥6.5 and control (RBG<110)**
p_3: p value for comparing between **RBG ≥110 & HBA1c <6.5and control (RBG<110)**

Table8a. Univariate analysis of risk factors associated with the occurrence of DM in dogs (n = 117)

Variables	N	Nondiabetic (n = 107)	Diabetic (n = 10)	OR (95% C.I)	p
Age (months)					
<12®	**36**	30 (83.3%)	6 (16.7%)		
12 m - <24	**26**	25 (96.2%)	1 (3.8%)	0.200 (0.023 – 1.774)	**0.148***
24 m - <48	**27**	27 (100%)	0 (0%)		
48 - <96	**22**	20 (90.9%)	2 (9.1%)	0.500 (0.092 – 2.730)	**0.423**
≥96	**6**	5 (83.3%)	1 (16.7%)	1.000 (0.098 – 10.166)	**1.000**
Gender					
Male®	**61**	57 (93.4%)	4 (6.6%)		**0.426**
Female	**56**	50 (89.3%)	6 (10.7%)	1.710 (0.456 – 6.407)	
Bread					
German Shepherd	**38**	35 (92.1%)	3 (7.9%)	0.882 (0.215 – 3.617)	**0.861**
Toy breeds	**23**	23 (100%)	0 (0%)		
Golden Retriever	**22**	19 (86.4%)	3 (13.6%)	1.985 (0.470 – 8.382)	**0.351**
Rottweiler	**7**	7 (100%)	0 (0%)		
Pitbull	**5**	3 (60%)	2 (40%)	8.667* (1.260 – 59.608)	**0.028***
Husky	**4**	4 (100%)	0 (0%)		
Cane Corso	**5**	4 (80%)	1 (20%)	2.861 (0.288 – 28.388)	**0.369**

Variables	N	Nondiabetic (n = 107)	Diabetic (n = 10)	OR (95% C.I)	p
Great Dane	**5**	4 (80%)	1 (20%)	2.861 (0.288 – 28.388)	**0.369**
Caucasian Shepherd	**1**	1 (100%)	0 (0%)		
Mastiff	**2**	2 (100%)	0 (0%)		
Doberman	**1**	1 (100%)	0 (0%)		
Labrador Retriever	**1**	1 (100%)	0 (0%)		
Dutch Shepherd	**0**	0 (%)	0 (0%)		
Saint Bernard	**1**	1 (100%)	0 (0%)		
Balady	**0**	0 (%)	0 (0%)		
Feeding Quality					
Balanced	**53**	48 (90.6%)	5 (9.4%)	1.229 (0.336 – 4.496)	**0.755**
More protein	**40**	35 (87.5%)	5 (12.5%)	2.057 (0.559 – 7.576)	**0.278**
More carb	**6**	6 (100%)	0 (0%)		
Sweets	**17**	17 (100%)	0 (0%)		
Dry food	**1**	1 (100%)	0 (0%)		
Feeding Quantity					
Balanced	**90**	82 (91.1%)	8 (8.9%)	1.220 (0.243 – 6.199)	**0.809**
Overeating ®	**27**	25 (92.6%)	2 (7.4%)		

®:Reference *: Statistically significant at p ≤ 0.2 OR: Odd`s ratio C.I: Confidence interval,

Table 8b. #Multivariate Logistic regression analysis of risk factors associated with DM in dogs in the study (n = 117)

Variables	p	β	OR	95%C.I
Age (months)				
<12®			**1.000**	
12 m - <24	**0.116**	**-2.024**	0.132	0.011 – 1.651
24 m - <48	**-**	**-**	-	-
48 - <96	**0.326**	**-0.958**	0.384	0.057 – 2.595
≥96	**0.900**	**0.150**	1.161	0.112 – 12.036
Bread				
German Shepherd	**0.122**	**-1.862**	0.435	0.609 –8.040
Toy breeds	**-**	**-**	-	-
Rottweiler	**-**	**-**	-	-
Golden Retriever	**0.081**	**0.226**	1.263	0.763 –12.5
Pitbull	**0.015***	**3.557**	35.048*	1.997 – 615.0
Husky	**-**	**-**	-	-
Cane Corso	**0.182**	**2.099**	4.160	0.374 – 78.10
Great Dane	**0.182**	**2.099**	4.160	0.374 – 78.10
Caucasian Shepherd	**-**	**-**	-	-
Mastiff	**-**	**-**	-	-
Doberman	**-**	**-**	-	-
Labrador Retriever	**-**	**-**	-	-
Dutch Shepherd	**-**	**-**	-	-
Saint Bernard	**-**	**-**	-	-
Balady	**-**	**-**	-	-
Caucasian Shepherd	**-**	**-**	-	-

OR: Odd`s ratio, C.I: Confidence interval, *: Statistically significant at $p \leq 0.05$
#: All variables with p≤0.2 was included in the multivariate β: regression coefficient

4. Discussion

In the present study, 32 dogs out of 139 (23%) were high for RBG (≥ 110mg/dl). Ten dogs (7.2 %) were high for HbA1c (≥ 6.5 %) with RBG≥ 200 mg/dl. This prevalence is so high compared to **Gilor et al. (2020) and Brito-Casillas et al. (2021),** who reported a prevalence of 0.6% and 0.56%, respectively, in a general dog population. This significant difference could be attributed to the fact that we selected the animals from the clinic, not from the general population. Also, we gave concern to those who had suspected clinical manifestations.

The current study shows the non-significant impact of DM on recurrent infections. It may be because all diabetic dogs in the study being completely vaccinated. When comparing diabetics to those with normal blood glucose levels, there was no significant difference in temperature or respiratory rate. However, there was a significant increase (p= 0.003) in pulse rate. Tachycardia may be due to anemia reported frequently among diabetics **(Marks and Kendall, 2018; Aldrich and Pauls, 2022)**. It may also be due to the autonomic dysfunction commonly found in diabetics that is associated with a high risk of cardiac arrhythmias, including tachycardia **(Leon and Maddox, 2015)**.

Diabetes Mellitus was significantly associated with weight loss (p < 0.001). These results are consistent with many studies **(Moshref et al., 2019; Shiel and Mooney, 2022).** May be due to the continuous loss of glucose in urine and the deficiency of the anabolic effect of insulin **(Toni et al, 201; Ziegler and Neu 2018; Shiel and Mooney, 2022).** The catabolic condition results from the changes in energy metabolism with severe energy store depletion as the body is forced to consume protein mass and fatty acids leading to weight loss **(Hebert and Nair 2010; Misra and Oliver 2015).**

Our study shows a significant association (p <0.001) between DM and increased appetite, polydipsia, and polyuria. This may be due to the great amount of water lost in the urine with glucose and the starvation state of the cells **(Ziegler and Neu, 2018).**

Our study declared that there was a significant impact of DM on the eyes of diseased dogs. Eighty percent of the diabetics suffer from cataract. This result is consistent with **(Wilkie et al., 2006; Miller and Brines 2018; Cantero et al., 2022).** This opacity appears due to the metabolism of glucose to its sugar alcohol "sorbitol" in the lens **(Varma, 1980)** which has a higher osmotic pressure absorbing water into the lens **(Hejtmancik et al., 2015)**. It may also be due to non-enzymatic glycation of the lens matter **(Hashim and Zarina, 2011)** or oxidation stress **(Williams, 2008).**

Regarding the impact of DM and high RBG levels on blood picture, although DM led to decreased Hb in large numbers of diabetic animals (70%) but the decrease in hemoglobin level was not significant. On the contrary, **Abdel-Moneim et al. (2020)** declared that DM led to anemia and revealed a significant reduction in hemoglobin and hematocrit values in T1DM. **Elie and Hoenig (1995)** reported that diabetes causes severe anemia in dogs. **Christopher (1995)** declared that diabetes causes hematologic abnormalities and affects blood cells, their metabolism, morphology, and function, and it also affects the coagulation system. Anemia may develop due to these complications. The non-significant decrease of hemoglobin in our study may be because

most of our cases are less than one year, and the complications, including anemia are not established yet.

DM had a significant impact on total leucocyte count (p <0.001). This result is consistent with **Abdel-Moneim et al. (2020),** who reported that there was a significant increase in total leukocyte count and in neutrophil count in newly diagnosed type 1 DM compared with a healthy control group and this may be due to the inflammation state and the oxidative stress markers. Precisely this point explains why in our study, the total leucocyte counts significantly increased despite the absence of infections. **Kashima et al. (2019)** declared that increased WBC counts were predictive of diabetes. On the contrary, **Mahdiani et al. (2019)** reported a non-significant association between WBC count and glycemic index.

However, there was no significant impact on platelet count. This is consistent with **Christopher (1995),** who did not find any effect of DM on platelets in his study. On the contrary, in the human study, **Abdel-Moneim et al. (2020)** reported a significant decrease in platelet count.

Regarding the impact of DM on liver function tests, we reported a non-significant increase in the mean values of AST and ALT in diabetics. This result coincided with **Lawrence et al. (2019)** who declared that dogs with DM rarely manifest liver dysfunction and lesser increases in transaminases activity, which may be because IDDM type 1 does not cause metabolic syndrome and fatty liver as NIDDM type 2 **(Starzl et al., 1975; Khoury et al., 2018; Chung et al., 2020)**.

There was a significant impact of DM on renal function where 70 % of the diabetics had impaired renal functions compared with 0% of the control group. The urea and creatinine values were significantly higher in diabetic group than in high RBG and control groups. These results were supported by **Herring et al. (2014)** who reported that the prevalence of elevated protein-creatinine ratio (UPC) and microalbuminuria in urine of diabetic dogs was up to 55% and 73%, respectively and **Wu et al. (2014)** who reported that the major leading cause of end-stage renal disease is diabetes. Several factors and mechanisms, including inflammation, oxidative stress, protein kinase C, advanced glycation end products, hyperglycemia, and poly (ADP-ribose) polymerase activation share to the pathogenesis and development of diabetic nephropathy **(Sun et al., 2013)**. **Novellas et al. (2008)** stated that in dogs, diabetes mellitus is a cause of hypertension associated with increases in vascular peripheral resistance leading to renal impairment.

As regard risk assessment study for DM in dogs, the current study reported that only age and breed were significant on the univariate analyses ($p \leq 0.2$) and subjected to multivariate logistic regression analyses, which revealed that only breed had been identified as a potential risk factor for DM in the dog. On the contrary, **Heeley et al. (2020)** recorded age, sex, and breed. Our study reported that dogs over 96 months showed 1.16 folds more risk of getting DM thanwith those <12 months. However, it is not significant. **Ringstad et al. (2022)** reported that their study's average age of DM cases was 8.8 years. **Guptill et al. (2003)** reported that DM was higher in dogs over ten years. **Heeley et al. (2020)** reported that DM is more commonly diagnosed in middle-aged dogs. In the current study, DM attacked 10.7% of entire female dogs compared with only 6.6% of males. However, the stepwise logistic regression model displayed that it was not a significant risk factor. This result was consistent with **Ringstad et al. (2022),** who reported that 62% of their diabetic dogs were females, and the research did not report if it is a significant risk factor.

On the contrary, **Brito-Casillas et al. (2021)** reported that entire female and castrated male dogs were at higher risk for DM compared with both desexed females and entire males. The higher percentage of DM in entire females than males may be because of progesterone and diabetogenic effect of growth hormone **(Koren, 2022)**. logistic regression analyses of our study revealed that only breed had been identified as a potential risk factor for DM in the dog. This result is consistent with **Heeley et al. (2020); Yoon et al. (2020) and Brito-Casillas et al. (2021),** who reported that some breeds are at high risk. **Ringstad et al. (2022)** reported that some dog breeds are more vulnerable to diabetes and others are less prone to the disease. There is a strong genetic susceptibility entangled in the aetiology of this disease. While our study reported that Pitbull breed had 35 folds more risk of getting diabetes compared with all others (p < 0.015; OR: 35.04; CI 95 % 1.997-615.0), **Ringstad et al. (2022)** reported that the 10 highest-ranked breeds included Australian Terrier which had the highest odds and also included the Swedish Lapphund, Samoyed, and West Highland White. However, neither of these breeds was enrolled in our study, and pitbull breed was not included in **Ringstad et al. (2022)** study. The same authors reported German Shepherds and Golden Retrievers as breeds that have the lowest odds for diabetes in their study, and this is consistent with our result about these two breeds. In the current study, feeding quality and quantity did not affect the incidence of diabetic cases. Canine DM is mainly insulin-dependent (type 1) and is not affected by providing as found in type 2 DM **(Matsubayashi et al. 2022, Song et al. 2022),** which increases by excessive carbohydrate intake **(Zhu et al., 2021).**

5. Conclusion

It can be concluded that the prevalence of DM among the studied dogs was 7.2%, and the clinical picture can be summarized in glycosuria, polyuria, polydipsia, polyphagia, and weight loss. There was a significant association between DM and an increase in pulse rate, cataract formation, abnormalities in total leucocyte count and impaired renal functions. Only breed that has been identified as a potential risk factor for canine DM.

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