

RESEARCH

Open Access



Diabetic retinopathy among Brazilian Xavante Indians

Carlos Gustavo M. G. Lima^{1*}, Laercio Joel Franco², Amaury L. Dal Fabbro², Edson Z. Martinez², João Paulo Botelho Veira-Filho³, Alexandre A. C. M. Ventura⁴, Leonardo Prevelato¹ and Antonio Augusto V. Cruz¹

Abstract

Background: To describe the frequency of diabetic retinopathy (DR) and its associated variables in Brazilian Xavante Indians.

Methods: A population-based survey carried out in two Xavante Reservations between 2008 and 2012, included 948 Indians aged 20 years or more, identified 246 individuals with type 2 diabetes. A non-probabilistic cluster sample of 140 diabetic individuals were submitted to ophthalmologic examination. Due to operational conditions and to optimize the field work, only the larger Xavante villages were included. Ophthalmologic examinations were performed during one trip to each reservation, in their villages and consisted of measurement visual acuity, anterior segment biomicroscopy, applanation tonometry, and direct and indirect ophthalmoscopy.

Results: The frequency of DR was 19.3%, distributed as follows: mild non-proliferative retinopathy in nine (33.3%) subjects, moderate in nine (33.3%), severe in six (22.3%), very severe in two (7.4%), and high-risk proliferative DR in one (3.7%). The occurrence of DR was higher among those with a longer duration of diabetes, higher levels of glycated hemoglobin (HbA1c) and fasting glucose, papillary excavation ≥ 0.5 , and among individuals in older age group. Using the log-binomial regression model, diabetes duration > 24 months and HbA1c $\geq 6.5\%$ were significantly associated with the occurrence of DR.

Conclusions: The presence of DR (19.3%) in Xavante Indians is an alert for health care providers for this population, since diabetes is a new disease among them. Its association with disease duration, high levels of HbA1c and blood glucose calls attention for the necessity of more actions to improve diabetes control in this recently contacted ethnic group that needs particular attention.

Keywords: Diabetes mellitus, Diabetic retinopathy, Indians, South American

Background

The prevalence of type 2 diabetes mellitus (T2DM) is increasing worldwide, and in some areas, the disease has reached epidemic status [1]. A distinctive characteristic of the epidemiology of this disease is the wide geographic and ethno-cultural variations in its prevalence. Indigenous people seem to be disproportionately affected, probably due to genetic susceptibility and lifestyle changes [2, 3]. The highest rates of diabetes were found

in natives of Nauru, a Pacific Island, and in Pima Indians in the United States, where the prevalence was as high as 50% [1].

Xavante is an indigenous population living in Mato Grosso State, central Brazil, belong to the Macro-Jê linguistic group, and having a low degree of admixture confirmed by genome wide analysis [4]. They comprise approximately 17,384 individuals [5, 6], distributed in nine Indian Reservations, making them one of the largest indigenous groups in Brazil [7]. Traditionally hunter-gatherers, due to conflict with newcomer farmers, they started to be settled in delimited areas since 1957. After the contact and subsequent acculturation process, they became more sedentary, and modified their traditional

*Correspondence: cgmglima@usp.br

¹ Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery, Ribeirão Preto Medical School, University of São Paulo, Av. Bandeirantes, 3900, Ribeirão Preto, SP 14049-900, Brazil
Full list of author information is available at the end of the article



diet by incorporating new foods, such as rice, sugar, and sweets [8]. Thus, important changes have been observed in the nutritional and health profile of this population, including diseases that were previously unknown to them, such as diabetes mellitus (DM) [9]. DM was first reported in the Xavante Indians in 1996 [10], when some members of the population sought medical assistance due to symptoms of metabolic decompensation and chronic DM complications [11].

The frequency of diabetic retinopathy (DR) among Xavante Indians is unknown. This survey aimed to describe the frequency of DR and potential risk factors for its development in this Brazilian Indian community.

Methods

This study involved Xavante Indians from the Sangradouro/Volta Grande and São Marcos reservations located in Mato Grosso, Brazil. According to the Brazilian 2013 Census [6], the total population living in Sangradouro/Volta Grande was 882 individuals (623 adults ≥ 20 years of age) in 31 villages, and the total population in São Marcos was 3138 individuals (1588 adults ≥ 20 years of age) living in 28 villages. A previous population-based survey conducted from 2008 through 2012, including 948 Xavante Indians aged 20 years or more, disclosed 246 (25.9%) subjects with T2DM who were included in this study [12]. A non-probabilistic cluster sample out of the 246 subjects with DM was selected, that is, only those from the larger villages, were invited to participate. This procedure was adopted due to operational conditions and to optimize the field work. The study sample was composed by 140 individuals, being 40 men and 100 women. Non-participation was mainly due to the nomadic characteristics of this population, and cultural habits, like hunting, that keep a substantial portion of the population, especially males, out of their homes.

Data collection

The collected information included the duration of DM, current DM treatment, smoking habits, anthropometric measurements (weight, height, waist circumference), blood pressure, capillary glycaemia (portable glucometer—*HemoCue*[®] *Glucose201*⁺ *HemoCue AB*, *Angelholm, Sweden*), blood and urine samples. Blood and urine samples were separated in aliquots and stored at -20 °C before transportation to the city of São Paulo for laboratory analyses. Diagnosis of DM was made if the individual had routine use of oral anti-diabetics or insulin, casual capillary glycemia ≥ 200 mg/dL, or a 2-h glucose level ≥ 200 mg/dL after a 75 g of glucose load, according to the World Health Organization (WHO) criteria [13]. The reference ranges used for laboratory tests were as follows: fasting glucose (abnormal ≥ 126 mg/dL); HbA1c

(abnormal $\geq 6.5\%$); total cholesterol (abnormal ≥ 200 mg/dL); HDL cholesterol (abnormal < 40 mg/dL for men or < 50 mg/dL for women); LDL cholesterol (abnormal ≥ 100 mg/dL); triglycerides (abnormal ≥ 150 mg/dL); apolipoprotein A-I (abnormal < 120 mg/dL); apolipoprotein B (abnormal ≥ 120 mg/dL); C-reactive protein (abnormal ≥ 3.0 mg/dL); and microalbuminuria (MA) (abnormal ≥ 30 mg/L). The anthropometric measurements included weight, height, and waist circumference (abdominal circumference measured halfway between the edge of the last rib and the iliac crest). The body mass index (BMI) was expressed as kg/m^2 . Comparisons of indigenous people and Caucasians in North America have reported no difference in the relationships between visceral adipose tissue and BMI [14], total body fat [15], or waist circumference [16]. Therefore, we used the standard criteria for the reference values in this population involving waist circumference (abnormal ≥ 102 cm for men or ≥ 88 cm for women and BMI normal < 25 ; overweight ≥ 25 and < 30 ; obesity ≥ 30). Blood pressure was measured in the left arm using seated patients, after 5 min of rest, using the Omron HEM 742INTCH. It was measured three times and the average of the last two readings was reported. Hypertension was defined as systolic blood pressure (SBP) equal to or more than 140 mmHg and/or diastolic blood pressure (DBP) equal to or more than 90 mmHg, according to the WHO criteria [17].

The ophthalmic examination was performed twice, the first in 2009 and the second in 2011, and comprised measurement of LogMAR visual acuity, anterior segment biomicroscopy (*Kowa SL-15*[®] portable slit-lamp), applanation tonometry (*Clement e Clarke*[®] Perkins tonometer), and a detailed fundus examination under mydriasis with indirect ophthalmoscopy (*Keeler wireless*[®] + 20D Aspheric Lens-*Volk*[®]). DR was graded according to the Early Treatment Diabetic Retinopathy Study (ETDRS), and categorised as follows: mild, moderate, severe, and very severe non-proliferative diabetic retinopathy (NPDR); early, high risk, and severe proliferative diabetic retinopathy (PDR) [18, 19].

Statistical analysis

Student's *t* tests were used to compare continuous clinical variables between two groups. Skewed variables were log transformed before these comparisons. Generalized linear regression with a log link and binomial distribution (log-binomial model) was used to assess the associations between clinical and demographic variables and the presence of retinopathy. These models are used to estimate crude and sex and age adjusted prevalence ratios (PR), with their associated 95% confidence intervals (95% CI). Associations were considered to be significant when

95% confidence intervals did not include 1 (similar to $p < 0.05$). The log-binomial models were fitted using the SAS software version 9.4.

The selection of a final subset of variables that best discriminate between individuals with and without DR used a conditional inference tree statistical modeling, a non-parametric class of multivariate regression model which embed tree-structured regression models into a well-defined theory of conditional inference procedures [20]. The use of conditional inference trees has several advantages in comparison with the traditional stepwise selection models, including: (a) conditional inference trees show details of the patterns of associations between the variables of interest, instead of only describing the variables that directly have associations with the dependent variable; and (b) continuous variables are directly inserted in the model and conditional inference procedures can define the optimal cut-off points for classifying individuals. The conditional inference trees were fitted with the package “party” of the software R version 3.4.3.

Results

From the 140 T2DM subjects examined, 27 (19.3%) had clinical signs of DR in at least one eye. According to the ETDRS classification [19], most patients had non-proliferative retinopathy classified as mild in nine (33.3%), moderate in nine (33.3%), severe in six (22.3%), and very severe in two (7.4%) patients. Only one case (3.7%) of high risk proliferative DR was diagnosed. Indirect signs of diabetic macular edema were observed in four (14.8%) patients.

Table 1 shows clinical and laboratory findings of the patients with T2DM according to the presence or absence of retinopathy. The occurrence of DR was higher among those with a longer duration of diabetes ($p < 0.01$), and higher levels of triglycerides ($p = 0.02$), HbA1c ($p < 0.01$), glucose ($p < 0.01$) and microalbuminuria ($p < 0.01$).

Table 2 shows the clinical characteristics of the patients with T2DM according to the presence or absence of diabetic retinopathy, and the correspondent age and sex adjusted prevalence ratios (PR) obtained from the log-binomial model. PR for fasting glycaemia and HbA1c were not obtained due to the presence of a zero value in the cross-tabulation. The occurrence of DR was higher in the age-group 40–59-years (27.1%) and 60 or more years (24.3%) than in the 20–39 years (4.6%). The occurrence of DR was also higher among those with longer duration of DM diagnosis and papillary excavation ≥ 0.5 . It was observed a non-significant crude association between DR and waist circumference (PR 1.7; 95% CI 0.8–3.4), but the sex and age adjusted PR indicates a significant association (PR 3.1; 95% CI 1.3–7.4). This difference between crude and adjusted PR suggests an interaction effect between waist circumference and sex or age groups. In fact, Table 3 shows that the association between waist circumference and DR is significant among women (PR 2.4; 95% CI 1.1–5.5), but this association is not significant among men (PR 1.7; 95% CI 0.3–7.6).

Multivariate analysis was conducted using a conditional inference tree to find the best model of variables associated with DR. All the variables showed in Table 2 were used as split conditions in this analysis, but the computational algorithm selected the duration of DM, the

Table 1 Diabetic retinopathy in Xavante Indians according to clinical and laboratory data

Variable	Diabetic retinopathy		p value ^a
	Yes (n = 27)	No (n = 113)	
	Mean (min–max)	Mean (min–max)	
Diabetes duration (months)	77.1 (12–180)	28.7 (0–132)	<0.01
Fasting glucose (mg/dL)	356.4 (230–600)	219.7 (72–600)	<0.01 ^b
Total cholesterol (mg/dL)	162.5 (124–280)	148.4 (15–378)	0.06 ^b
Triglycerides (mg/dL)	309.9 (88–3654)	220.3 (53–1981)	0.02 ^b
HDL cholesterol (mg/dL)	40.0 (26.0–63.0)	39.3 (23.6–59.0)	0.63 ^b
LDL cholesterol (mg/dL)	75.4 (10–140)	69.2 (27–116)	0.32
C-reactive protein (mg/L)	2.92 (0.48–41.44)	3.78 (0.35–83.05)	0.28 ^b
HbA1c (%)	12.5 (8.2–16.0)	9.76 (5.5–18.8)	<0.01 ^b
Microalbuminuria (mg/L)	49.8 (2.2–778)	17.2 (1.1–5190)	<0.01 ^b
Apolipoprotein A-I (mg/dL)	114.1 (96.8–143)	110.7 (73–229.2)	0.23 ^b
Apolipoprotein B (mg/dL)	71.4 (30.4–113)	75.2 (38–134)	0.42 ^b

^a Student's t test for mean comparison

^b Data were transformed in logarithmic values to a skewed distribution. In these cases, data are described by geometric means

Table 2 Frequency of diabetic retinopathy in Brazilian Xavante Indians according to clinical data and age and sex adjusted prevalence ratios

	Total	Diabetic Retinopathy		Crude PR (95% CI)	Adjusted PR (95% CI)
		n	%		
Age (years)					
18–39	44	2	4.6	Reference	Reference
40–59	59	16	27.1	6.0 (1.4–24.6)*	6.3 (1.5–26.2)*
60 or more	37	9	24.3	5.3 (1.2–23.2)*	5.4 (1.2–23.5)*
Sex					
Men	40	7	17.5	Reference	Reference
Women	100	20	20.0	1.1 (0.5–2.5)	1.4 (0.6–3.0)
Duration of DM					
≤ 24 months	73	2	2.7	Reference	Reference
25–108 months	57	17	29.8	10.9 (2.6–45.2)*	2.3 (1.4–3.7)*
> 108 months	10	8	80.0	29.2 (7.2–118.6)*	3.8 (2.0–7.0)*
Smoking					
Yes	15	1	6.7	Reference	Reference
No	125	26	20.8	3.1 (0.4–21.4)	2.6 (0.3–17.7)
Waist circumference					
Abnormal	104	17	16.4	Reference	Reference
Normal	36	10	27.8	1.7 (0.8–3.4)	3.1 (1.3–7.4)*
BMI (kg/m ²)					
< 25	19	6	31.6	Reference	Reference
25–29.9	51	13	25.5	0.8 (0.3–1.8)	0.5 (0.2–1.4)
≥ 30	70	8	11.4	0.4 (0.1–0.9)*	0.3 (0.1–0.8)*
Hypertension					
No	116	24	20.7	Reference	Reference
Yes	24	3	12.5	0.6 (0.1–1.8)	0.5 (0.1–1.5)
Cataract					
No	103	16	15.5	Reference	Reference
Yes	37	11	29.7	1.9 (0.9–3.7)	1.8 (0.8–4.1)
Papillary excavation					
0.1–0.4	128	21	16.4	Reference	Reference
0.5–0.9	12	6	50.0	3.0 (1.5–6.1)	2.7 (1.3–5.4)*
Visual acuity					
0–0.5	117	21	18.0	Reference	Reference
0.6–0.9	17	4	23.5	1.3 (0.5–3.4)	1.0 (0.3–2.7)
≥ 1	5	2	40.0	2.2 (0.7–7.0)	1.8 (0.6–5.3)
Fasting glycemia					
< 140 mg/dL	35	0	0	Reference	
140 mg/dL	105	27	25.7		
Total cholesterol					
< 200 mg/dL	121	25	20.7	Reference	Reference
≥ 200 mg/dL	15	2	13.3	0.6 (0.1–2.5)	0.7 (0.2–2.8)
HDL					
Normal	24	5	20.8	Reference	Reference
Abnormal	112	22	19.6	0.9 (0.3–2.2)	0.7 (0.2–1.7)
Triglycerides					
< 150 mg/dL	32	2	6.2	Reference	Reference
≥ 150 mg/dL	104	25	24.0	3.9 (0.9–15.3)	3.7 (0.9–14.7)

Table 2 (continued)

	Total	Diabetic Retinopathy		Crude PR (95% CI)	Adjusted PR (95% CI)
		n	%		
LDL					
< 100 mg/dL	101	18	17.8	Reference	Reference
≥ 100 mg/dL	14	2	14.3	0.8 (0.2–3.1)	0.8 (0.2–3.2)
C-reactive protein					
Normal	61	14	23.0	Reference	Reference
Abnormal	75	13	17.3	0.7 (0.3–1.5)	0.7 (0.3–1.4)
HbA1c (%)					
< 6.5	20	0	0	Reference	
≥ 6.5%	104	27	26.0		
Microalbuminuria					
Normal	76	13	17.1	Reference	Reference
Abnormal	45	14	31.1	1.8 (0.9–3.5)	1.9 (1.0–3.5)

*Significant at $p < 0.05$ **Table 3 Association between waist circumference and DR stratified by sex**

Sex	Waist circumference	Total	Diabetic Retinopathy		PR (95% CI)
			n	%	
Men	Abnormal	16	2	12.5	Reference
	Normal	24	5	20.8	1.7 (0.3–7.6)
Women	Abnormal	88	15	17.1	Reference
	Normal	12	5	41.7	2.4 (1.1–5.5)*

*Significant at $p < 0.05$

microalbuminuria and the papillary excavation as those most able to jointly classify between individuals with and without DR (Fig. 1). For a better clinical interpretation, Table 4 shows the probabilities of DR considering the set of variables selected in the multivariate analysis, but considering the traditional reference ranges for each variable (MA values classified as abnormal if ≥ 30 mg/L, and papillary excavation classified according to the intervals 0.1–0.4 and 0.5–0.9).

Discussion

The Xavante Indians formed a genetically isolated population, with a low degree of miscegenation. The interaction between genetic susceptibility and changes in lifestyle is considered the main reason for the outbreak of a diabetes epidemic in this population [4, 12].

An early onset of T2DM (age of diagnosis < 40 years of age) has become increasingly prevalent, with a significant impact on the health care of these individuals. Obesity, a family history of T2DM, sedentary lifestyle, an ethnic minority, and female gender are some of the potential risk

factors for this condition [21]. In an ongoing prospective cohort study in Asia, including 41,019 participants from nine countries, the overall rate of T2DM was 18% [22] versus 36.2% among the Xavante Indians [12]. Patients with early-onset T2DM are associated with an increased risk of premature development of microvascular and macrovascular complications [21]. The risk of developing premature retinopathy in these patients resulted predominantly from hypertension and prolonged exposure to suboptimal diabetes treatment [23].

A variety of techniques can be used to detect and classify diabetic retinopathy, including direct and indirect ophthalmoscopy, stereoscopic color fundus photography, fluorescein angiography, and mydriatic or nonmydriatic digital color or monochromatic photography [24]. Ophthalmoscopy is the most commonly used technique to screen for diabetic retinopathy. However, has lower sensitivity relative to gold standard 7-field stereoscopic color photography as defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) group [25].

The estimated overall prevalence of DR for 2010 in a systematic literature review conducted between 1980 and 2008 was 34.6% for any DR [26]. The current prevalence of DR in any Brazilian Indian population is unknown. In this study, the frequency of DR among Xavante Indians was 19.3%, lower than the reported prevalence of DR in the Brazilian population of 19.5–42.9% [27–31], which was lower than that in some indigenous populations in North America and Australia [32–35]. Table 1 shows that the average DM duration was 77.1 months in patients with DR versus only 28.7 months for subjects without DR. It is possible that the relatively short duration of the disease associated to lower sensitivity of funduscopy to detect minimal changes such as microaneurysms,

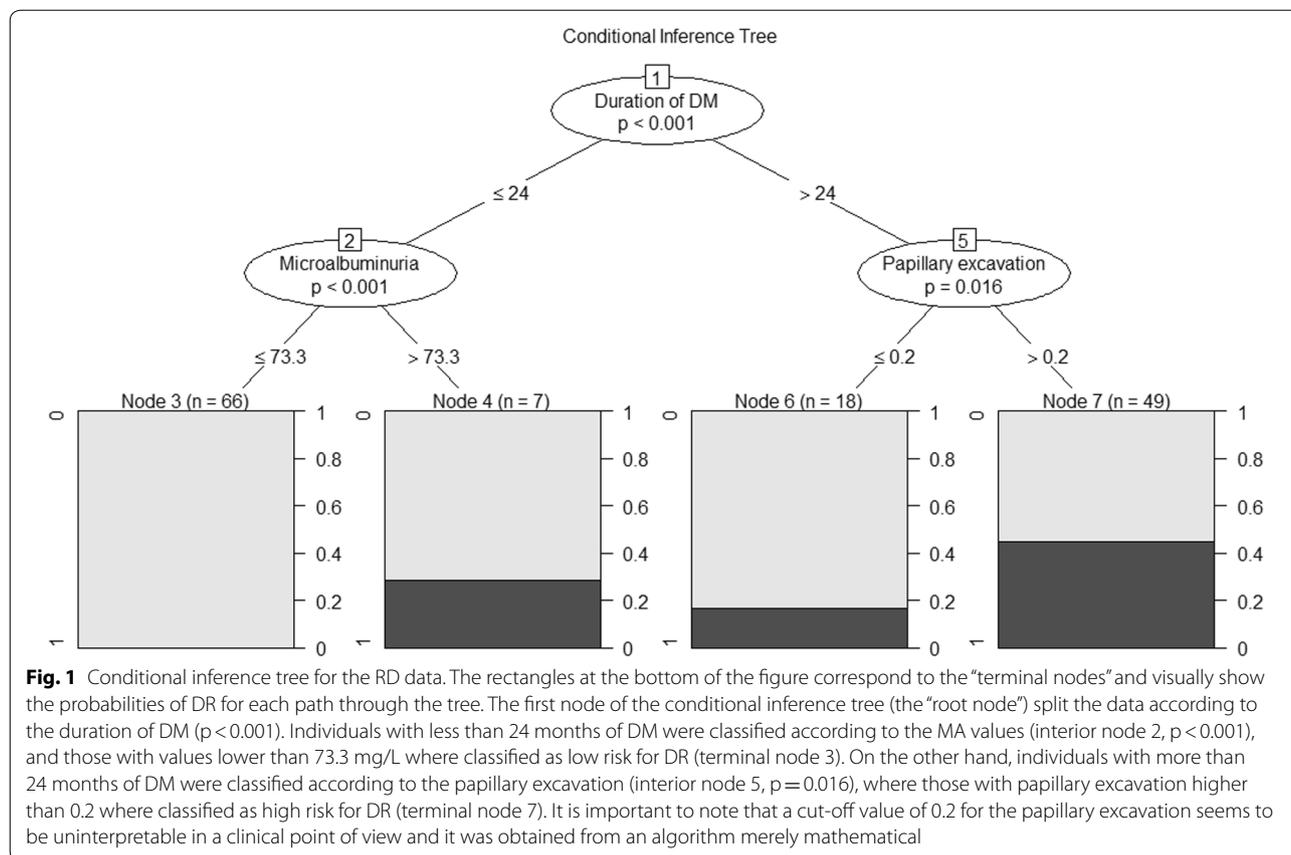


Table 4 Association pattern between duration of DM, MA, papillary excavation and DR

Duration of DM	Total	Diabetic retinopathy	
		n	%
≤ 24 months			
Microalbuminuria normal	40	0	0
Microalbuminuria abnormal	17	2	11.8
> 24 months			
Papillary excavation 0.1–0.4	60	20	33.3
Papillary excavation 0.5–0.9	7	5	71.4

contributed to the lower rate of retinopathy in this population. Among Xavante Indians, the frequency of DR was significantly higher among those with DM duration ≥ 108 months than among those with duration less or equal to 24 months (adjusted PR = 3.8, 95% CI 2.0–7.0; Table 2).

The prevalence of diabetic macular edema (DME) is continuously rising worldwide and has become one of the major causes of vision loss in the working-age

population. The gold standard in diagnosing DME still remains fluorescein angiography (FA). The optical coherence tomography (OCT) also can be used for screening, classification, monitoring, and treatment evaluation of DME [36]. Although funduscopy does not allow adequate detection of DME, when compared to the methods described above, we found in this study four (14.8%) patients with clinical signs of macular edema.

Glycemic control is the most important independent risk factor for DR [37]. Several studies have identified an association between poor glucose control and an increased occurrence of DR [38–41]. In the present study, all 27 patients with DR had elevated levels of fasting glucose and HbA1c, reflecting poor metabolic control.

The diagnosis of glaucoma is traditionally based on the finding of optic nerve head (ONH) damage assessed subjectively by ophthalmoscopy or photography or by corresponding damage to the visual field assessed by automated perimetry, or both [42]. The stereoscopic optic nerve head photograph is the most accurate method for papillary excavation quantification and common imaging devices outperform most clinicians in classifying optic discs [43]. Although ophthalmoscopy is not the standard method for papillary excavation quantification, in

this study, all patients who presented papillary excavation ≥ 0.5 and/or any other suspected alteration of the optic disc observed at ophthalmoscopy, were referred for investigation. Epidemiological studies have reported an association between DM and open-angle glaucoma [44–47]. Although this association is not fully understood, it is believed that DM causes microvascular flow impairment in the anterior portion of the optic nerve [48, 49]. In this study, it was not possible to determine which patients presented the diagnosis of glaucoma and whether there would be an association between this variable and DR. Despite this, the occurrence of DR was higher among those with papillary excavation ≥ 0.5 (adjusted PR = 2.7, 95% CI 1.3–5.4; Table 2).

Hypertension is a very common comorbidity in DM, affecting approximately 20–60% of these patients [50]. A previous study reported that the prevalence of hypertension among Xavante Indians was 17.5% [12], which was lower than the 20% found in the general adult Brazilian population [51]. Several studies have reported an association of hypertension with DR [32, 52–55]. Despite the report of this association, it was not found among the Xavante Indians (adjusted PR = 0.5, 95% CI 0.1–1.5; Table 2). However, this finding needs to be confirmed because the small sample size may have biased the results.

Although there are reports of an association of DR with other variables such increased levels of total cholesterol [56] and triglycerides [57], we could not find association of total cholesterol or its fractions with DR in the Xavante population, but individuals with DR had mean values of triglycerides higher than individuals without the disease ($p = 0.02$; Table 1).

Diabetic nephropathy develops in approximately 20–40% of type 1 diabetic patients and in less than 20% of type 2 diabetic patients [58]. Past studies have reported an association between DR and MA [59, 60]. In the present study, we found 14 patients who developed MA and diabetic retinopathy, 13 patients who developed retinopathy but not MA, and 33 patients who developed only MA. Initially, we found no association between MA and diabetic retinopathy (adjusted PR = 1.9, 95% CI 1.0–3.5; Table 2). However, the multivariate analysis using a conditional inference tree evidenced that MA is statistically associated with DR only for the Xavante Indians with less than 24 months of DM ($p < 0.001$, Fig. 1).

There are limitations to this study. A major limitation was low participation in the study (56%), which may have biased some of the results. Individuals from small villages were not included in the ophthalmologic survey to optimize the field work carried out in two visits. The lower sensitivity of fundoscopy to detect minimal changes may also have contributed to the lower rate of retinopathy in

this population. The small number of cases ($n = 27$) also reduced the power to detect associations. The poor diabetes control for a prolonged period of time may have influenced the relationship between some variables as weight excess, waist circumference, sex and DR. The presence of DR is also an indicator that other chronic diabetes complications are being developed.

Conclusion

The presence of DR (19.3%) in Xavante Indians is an alert for health care providers for this population, since diabetes is a new disease among them. Its association with disease duration, high levels of HbA1c and blood glucose calls attention for the necessity of more actions to improve diabetes control in this recently contacted ethnic group that needs particular attention.

Abbreviations

DR: diabetic retinopathy; HbA1c: glycated hemoglobin; DM: diabetes mellitus; T2DM: type 2 diabetes mellitus; MA: microalbuminuria; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; WHO: World Health Organization; ETDRS: Early Treatment Diabetic Retinopathy Study; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; DME: diabetic macular edema; FA: fluorescein angiography; OCT: optical coherence tomography; ONH: optic nerve head.

Authors' contributions

Conceived and designed the study: CGMGL, LJF, ALDF, AAVC. Collected data: CGMGL, LJF, ALDF, JPBVF, AACMV, LP. Analyzed the data: CGMGL, LJF, EZM. Wrote the manuscript: CGMGL, LJF, EZM, AAVC. All authors read and approved the final manuscript.

Author details

¹ Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery, Ribeirão Preto Medical School, University of São Paulo, Av. Bandeirantes, 3900, Ribeirão Preto, SP 14049-900, Brazil. ² Department of Social Medicine, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, SP 14049-900, Brazil. ³ Division of Endocrinology, São Paulo Medical School, Federal University of São Paulo, São Paulo, SP 04038-001, Brazil. ⁴ Department of Ophthalmology, Fernando Ventura Eye Institute, Recife, PE 52010-140, Brazil.

Acknowledgements

The authors would like to thank the Catholic Salesian Mission and Xavante indigenous community from the Sangradouro/Volta Grande and São Marcos reservations for the collaboration received through the development of this study.

Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was approved by the Brazilian National Indian Foundation Agency that is responsible for indigenous protection, as well as by the Ethics Committee of the Ribeirão Preto Medical School, and the Brazilian National Ethics Committee of the Ministry of Health, in accordance with the declaration of

Helsinki. The local ethics committee approved the study protocol and written informed consent was obtained from all patients or their legal representative.

Funding

This study was supported by the Fundação de Amparo à Pesquisa do Estado de São Paulo-FAPESP (proc. 2010/05634-0) and the Conselho Nacional de Desenvolvimento Científico e Tecnológico-CNPq (proc. 476347/2007-6).

Prior publication

This submission has not been published anywhere previously and it is not simultaneously being considered for any other publication.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 26 March 2018 Accepted: 1 June 2018

Published online: 13 June 2018

References

- Gadsby R. Epidemiology of diabetes. *Adv Drug Deliv Rev.* 2002;54:1165–72.
- Naqshbandi M, Harris SB, Esler JG, Antwi-Nsiah F. Global complication rates of type 2 diabetes in Indigenous peoples: a comprehensive review. *Diabetes Res Clin Pract.* 2008;82:1–17.
- Yu CH, Zinman B. Type 2 diabetes and impaired glucose tolerance in aboriginal populations: a global perspective. *Diabetes Res Clin Pract.* 2007;78:159–70.
- Kuhn PC, Horimoto AR, Sanches JM, Vieira Filho JP, Franco L, Fabbro AD, et al. Genome-wide analysis in Brazilian Xavante Indians reveals low degree of admixture. *PLoS ONE.* 2012;7:e42702.
- Lima CGMG. Saúde ocular em índios Xavante portadores de diabetes mellitus tipo 2 [Doctoral thesis]: São Paulo University; 2015.
- Brasil, Ministério da Saúde (MS), Fundação Nacional de Saúde (FUNASA). Sistema de Informações da Atenção à Saúde Indígena (SIASI). Relatório pirâmide populacional indígena. 2013. <http://portals.saude.gov.br/saude-indigena/gestao/siasi>. Accessed 24 Mar 2018.
- Pereira NOM, Santos RV, Welch JR, Souza LG, Coimbra CE Jr. Demography, territory, and identity of indigenous peoples in Brazil: the Xavante Indians and the 2000 Brazilian National Census. *Hum Org.* 2009;68:166–80.
- Arantes R, Santos RV, Coimbra Jr CEA. Saúde bucal na população indígena Xavante de Pimentel Barbosa, Mato Grosso, Brasil. *Cad Saúde Pública.* 2001;17:375–84.
- Coimbra CE Jr, Flowers NM, Salzano FM, Santos RV. The Xavante in transition: health, ecology and bioanthropology in Central Brazil. Ann Arbor: University of Michigan Press; 2002.
- Vieira Filho JP. Emergência do diabetes melito tipo II entre os Xavantes. *Rev Ass Med Brasil.* 1996;42:61.
- Vieira Filho JP, Franco LJ. Prevalência de diabetes mellitus em índios Xavante de Sangradouro-MT. *Arq Bras Endocrinol Metabol.* 2007;51:5492.
- Dal Fabbro AL, Franco LJ, da Silva AS, Sartorelli DS, Soares LP, Franco LF, et al. High prevalence of type 2 diabetes mellitus in Xavante Indians from Mato Grosso, Brazil. *Ethn Dis.* 2014;24:35–40.
- World Health Organization. World Health Organization definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1: diagnosis and classification of diabetes mellitus. WHO/NCS/99.2. Geneva: WHO; 1999.
- Gautier JF, Milner MR, Elam E. Visceral adipose tissue is not increased in Pima Indians compared with equally obese Caucasians and is not related to insulin action or secretion. *Diabetologia.* 1999;42:28–34.
- Lear SA, Humphries KH, Kohli S. Visceral adipose tissue accumulation differs according to ethnic background: results of the Multicultural Community Health Assessment Trial (M-CHAT). *Am J Clin Nutr.* 2007;86:353–9.
- Lear SA, Humphries KH, Frohlich JJ. Appropriateness of current thresholds for obesity-related measures among Aboriginal people. *Can Med Assoc J.* 2007;177:1499–505.
- Chalmers J. 1999 World Health Organization-International Society of Hypertension guidelines for the management of hypertension. Guidelines subcommittee. *J Hypertens.* 1999;17:151–83.
- Aiello LM. Perspectives on diabetic retinopathy. *Am J Ophthalmol.* 2003;136:122–35.
- Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. *Ophthalmology.* 1991;98:823–33.
- Speybroeck N. Classification and regression trees. *Int J Public Health.* 2012;57:243–6.
- Wilmot E, Idris I. Early onset type 2 diabetes: risk factors, clinical impact and management. *Ther Adv Chronic Dis.* 2014;5:234–44.
- Yeung RO, Zhang Y, Luk A, Yang W, Sobrepena L, Yoon KH, et al. Metabolic profiles and treatment gaps in young-onset type 2 diabetes in Asia (the JADE programme): a cross-sectional study of a prospective cohort. *Lancet Diabetes Endocrinol.* 2014;2:935–43.
- Song SH, Gray TA. Early-onset type 2 diabetes: high risk for premature diabetic retinopathy. *Diabetes Res Clin Pract.* 2011;94:207–11.
- Fong DS, Aiello LP, Ferris FL 3rd, Klein R. Diabetic retinopathy. *Diabetes Care.* 2004;27:2540–53.
- Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs—an extension of the modified Airlie House classification. ETDRS report number 10. *Ophthalmology.* 1991;98:786–806.
- Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care.* 2012;35:556–64.
- Escarião PHG, Arantes TEF, Filho NCF, Urtiga RD, Florêncio TLT, Arcoverde ALAL. Epidemiologia e diferenças regionais da retinopatia diabética em Pernambuco. *Brasil Arq Bras Oftalmol.* 2008;71:172–5.
- Garcia CAA, Gomes AHB, Nunes IM, Oliveira TL, Monteiro J. Diabetic retinopathy incidence and risk factors in patients of the Onofre Lopes University Hospital, Natal—RN. *Arq Bras Oftalmol.* 2003;66:355–8.
- Guedes MF, Portes AJF, Couto AF Jr, Nunes JS, Oliveira RCC. Prevalência da retinopatia diabética em unidade do programa de saúde da família. *Rev Bras Oftalmol.* 2009;68:90–5.
- Jost BS, Hilgemberg E, Rodrigues EB, Daniotti AF, Bonamico EL [Prevalence of diabetic retinopathy in patients affected by type 2 diabetes mellitus in the city of Luzerna—SC. *Arq Bras Oftalmol.* 2010;73:259–65.
- Drummond KRG, Malerbi FK, Morales PH, Mattos TCL, Pinheiro AA, Mallmann F, et al. Regional differences in the prevalence of diabetic retinopathy: a multi center study in Brazil. *Diabetol Metab Syndr.* 2018;10:1–11.
- Berinstein DM, Stahn RM, Welty TK, Leonardson GR, Herlithy JJ. The prevalence of diabetic retinopathy and associated risk factors among Sioux Indians. *Diabetes Care.* 1997;20:757–9.
- Farrell MA, Quiggins PA, Eller JD, Owle PA, Miner KM, Walkingstick ES. Prevalence of diabetes and its complications in the Eastern Band of Cherokee Indians. *Diabetes Care.* 1993;16:253–6.
- Ross SA, McKenna A, Mozejko S, Fick GH. Diabetic retinopathy in native and nonnative Canadians. *Exp Diabetes Res.* 2007;2007:76271.
- Maberley D, Walker H, Koushik A, Cruess A. Screening for diabetic retinopathy in James Bay, Ontario: a cost-effectiveness analysis. *CMAJ.* 2003;168:160–4.
- Schmidt-Erfurth U, Garcia-Arumi J, Bandello F, Berg K, Chakravarthy U, Gerendas BS, et al. Guidelines for the management of diabetic macular edema by the european society of retina specialists (EURETINA). *Ophthalmologica.* 2017;237:185–222.
- Kulberg CE, Arnqvist HJ. Good blood glucose control characterizes patients without retinopathy after long diabetes duration. *Diabet Med.* 1994;12:314–20.
- Diabetes Control and Complications Trial Research Group. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial. *Diabetes.* 1995;44:968–83.
- Cheng YJ, Gregg EW, Geiss LS, Imperatore G, Williams DE, Zhang X, et al. Association of A1C and fasting plasma glucose levels with diabetic retinopathy prevalence in the U.S. population: implications for diabetes diagnostic thresholds. *Diabetes Care.* 2009;32:2027–32.
- Frank RN, Hoffman WH, Podgor MJ, Joondeph HC, Lewis RA, Margherio RR, et al. Retinopathy in juvenile-onset type I diabetes of short duration. *Diabetes.* 1982;31:874–82.

41. Fong DS, Ferris FL 3rd, Davis MD, Chew EY. Causes of severe visual loss in the early treatment diabetic retinopathy study: ETDRS report no. 24. Early Treatment Diabetic Retinopathy Study Research Group. *Am J Ophthalmol*. 1999;127:137–41.
42. Michelessi M, Lucenteforte E, Oddone F, Brazzelli M, Parravano M, Franchi S, et al. Optic nerve head and fibre layer imaging for diagnosing glaucoma. *Cochrane Database Syst Rev*. 2015;11:CD008803.
43. Reus NJ, Lemij HG, Garway-Heath DF, Airaksinen PJ, Anton A, Bron AM, et al. Clinical assessment of stereoscopic optic disc photographs for glaucoma: the European Optic Disc Assessment Trial. *Ophthalmology*. 2010;117:717–23.
44. Chopra V, Varma R, Francis BA, Wu J, Torres M, Azen SP, et al. Type 2 diabetes mellitus and the risk of open-angle glaucoma the Los Angeles Latino Eye Study. *Ophthalmology*. 2008;115(227–32):e1.
45. Klein BE, Klein R, Jensen SC. Open-angle glaucoma and older-onset diabetes. The Beaver Dam Eye Study. *Ophthalmology*. 1994;101:1173–7.
46. Klein BE, Klein R, Moss SE. Intraocular pressure in diabetic persons. *Ophthalmology*. 1984;91:1356–60.
47. Zhou M, Wang W, Huang W, Zhang X. Diabetes mellitus as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. *PLoS ONE*. 2014;9:e102972.
48. Flammer J, Orgul S, Costa VP, Orzalesi N, Kriegelstein GK, Serra LM, et al. The impact of ocular blood flow in glaucoma. *Prog Retin Eye Res*. 2002;21:359–93.
49. Piltz-seymour JR, Grunwald JE, Hariprasad SM, Dupont J. Optic nerve blood flow is diminished in eyes of primary open-angle glaucoma suspects. *Am J Ophthalmol*. 2001;132:63–9.
50. American Diabetes Association. American diabetes association: treatment of hypertension in adults with diabetes. *Diabetes Care*. 2002;25:S71–3.
51. Passos VMA, Assis TD, Barreto SM. Hypertension in Brazil: estimates from population-based prevalence studies. *Epidemiol Serv Saúde*. 2006;15:35–45.
52. Bertelsen G, Peto T, Lindekleiv H, Schirmer H, Solbu MD, Toft I, et al. Sex differences in risk factors for retinopathy in non-diabetic men and women: the Tromso Eye Study. *Acta Ophthalmol*. 2014;92:316–22.
53. Klein R, Klein BE, Moss SE, Cruickshanks KJ. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: XVII. The 14-year incidence and progression of diabetic retinopathy and associated risk factors in type 1 diabetes. *Ophthalmology*. 1998;105:1801–15.
54. Moreno A, Lozano M, Salinas P. Diabetic retinopathy. *Nutr Hosp*. 2013;28(Suppl 2):53–6.
55. Xu J, Wei WB, Yuan MX, Yuan SY, Wan G, Zheng YY, et al. Prevalence and risk factors for diabetic retinopathy: the Beijing communities diabetes study 6. *Retina*. 2012;32:322–9.
56. Chew EY, Klein ML, Ferris FL 3rd, Remaley NA, Murphy RP, Chantry K, et al. Association of elevated serum lipid levels with retinal hard exudate in diabetic retinopathy. Early Treatment Diabetic Retinopathy Study (ETDRS) Report 22. *Arch Ophthalmol*. 1996;114:1079–84.
57. Minuto N, Emmanuele V, Vannati M, Russo C, Rebori C, Panarello S, et al. Retinopathy screening in patients with type 1 diabetes diagnosed in young age using a non-mydriatic digital stereoscopic retinal imaging. *J Endocrinol Invest*. 2012;35:389–94.
58. Jawa A, Kcomt J, Fonseca VA. Diabetic nephropathy and retinopathy. *Med Clin N Am*. 2004;88:1001–36.
59. Klein R. The epidemiology of diabetic retinopathy. *Diabet Retinopath*. Baltimore: Human Press; 2008.
60. Wang J, Zhang RY, Chen RP, Sun J, Yang R, Ke XY, et al. Prevalence and risk factors for diabetic retinopathy in a high-risk Chinese population. *BMC Public Health*. 2013;13:633.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

