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The feasibility of smartphone based retinal photography for diabetic retinopathy screening among Brazilian Xavante Indians

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ABSTRACT

Aims: To evaluate the feasibility of smartphone based retinal photography for diabetic retinopathy (DR) screening among Brazilian Xavante Indians and the yield of retinal images.

Methods: A non-probabilistic cluster sample of 170 individuals with and without diabetes was enrolled for ocular examination with a portable retinal camera during DR screening at two Xavante Reservations. Due to operational conditions and to optimize the field work, only the larger Xavante villages were included. Images were obtained after pupil dilation; image analysis included assessment of quality, presence of media opacities and diabetic retinopathy grading whenever possible for individuals with diabetes.

Results: A total of 157 individuals underwent the complete ocular imaging protocol, 95 with diabetes (60.5%). Among those with diabetes, 23 (24.2%) could not have DR graded because of media opacities. For those with gradable images, the frequency of DR was 22.2%; sight-threatening DR was present in 9.7%. The main causes for ungradable images were cataracts and asteroid hyalosis.

Conclusions: The presence of DR was higher than in previous studies, calling attention for its prevention in this vulnerable population. The screening model with a smartphone-based portable retinal camera is feasible and could increase screening coverage if associated with telemedicine.

1. Introduction

Xavante is a genetically isolated indigenous population living

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in Mato Grosso State, central Brazil [1]. They are one of the largest indigenous groups in Brazil, with approximately 17,000 individuals, distributed in nine Indian Reservations. Traditionally hunters-gatherers, they started to be settled in delimited areas in the late 1950s, having become more sedentary, and modifying their traditional diet by incorporating new foods, such as rice, sugar, and sweets. 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) [2].

To screen for diabetic retinopathy (DR) in underserved areas in general and in indigenous populations in particular is considered a challenge; the epidemic of DM in the Xavante urges a solution for adequately examining all individuals with DM and timely referring those with sight-threatening DR for treatment. Digital retinal photography and telemedicine have been proposed for such screening in underserved areas [3].

The objectives of the present study were to evaluate the feasibility and yield of smartphone based retinal photography for diabetic retinopathy screening among Brazilian Xavante Indians.

2. Materials and methods

2.1. Subjects

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, the total population living in Sangradouro/ Volta Grande was 882 individuals (623 adults $\geq$ 20 years of age) in 31 villages, and the total population in São Marcos was 3138 individuals (1588 adults $\geq$ 20 years of age) living in 28 villages. [2] 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 [4].

In this setting, ophthalmological examination was offered at two Xavante Reserves in January 2020, primarily for the screening of diabetic retinopathy. Some villages were selected due to operational conditions in order to optimize field work. Due to the scarcity of ocular health professionals in the region, there was a demand for routine ocular examination even for non-diabetic individuals; a total of 170 individuals (60.9% with diabetes) were enrolled for ocular examination, being 80 men and 90 women.

2.2. Data collection

The collected information included presence of DM, DM duration, and blood pressure measurements. Diagnosis of DM was made if the individual had routine use of oral anti-diabetics or insulin, casual capillary glycemia $\geq$ 200 mg/dL, or a 2-h glucose level $\geq$ 200 mg/dL after a 75 g of glucose load, according to the World Health Organization (WHO) criteria [5]. Blood pressure was measured in the right arm in sitting position, 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 [6]; hypertension diagnosis was also considered in patients under oral treatment with anti-hypertensive drugs.

The ophthalmic examination comprised of anamnesis, tonometry (HA-2 portable applanation tonometer, Kowa American Corporation, Torrance, USA) and photographs of the anterior and posterior ocular segments (Eyer, Phelcom Technologies, São Carlos, Brazil) after mydriasys, obtained with 1% tropicamide drops. Image acquisition was performed by an ophthalmologist with previous experience on retinal imaging. Intraocular pressure (IOP) was considered normal if values fell within 10–21 mmHg range. The evaluation of the posterior segment comprised two photographs of each fundus, one field centered on the fovea and the other field centered on the optic disc (Fig. 1).

Anterior ocular segment was subsequently analyzed regarding presence of pterygium, cataracts and media opacities; cataract was graded as severe when its presence precluded the fundus evaluation. Fundus photographs were analyzed regarding the media transparence, image quality and DR grading, as described elsewhere [3]; briefly, each patient was categorized according to the most affected eye as follows: mild, moderate, and severe non-proliferative diabetic retinopathy (NPDR); proliferative diabetic retinopathy (PDR); presence of macular edema (ME). Sight-threatening DR (STDR) was defined when either severe NPDR, PDR or ME were present in at least one eye. All images were analyzed on-site by a single retina specialist (FKM).

The Indian leaders and the study participants were informed about the purposes of this study and gave their consent. A Xavante health agent worked as an interpreter when necessary. This study is part of a broader investigation approved by Ethics Committee of Ribeirao Preto Medical School, University of Sao Paulo, Brazil and Brazilian National Ethics Commision (CONEP).

2.3. Statistical analysis

All data were collected in MS Excel 2010 files (Microsoft Corporation, Redmond, WA, USA). Statistical analyses were performed with SPSS 19.0 for Windows (SPSS Inc., Chicago, IL, USA). Patient's characteristics and quantitative variables are presented in terms of mean and standard deviation (SD). A paired 2-tailed Student *t*-test was used to compare continuous clinical variables between the two groups. Fisher's exact or Chi square tests were used for unpaired variables. The 5% level of significance was used.

3. Results

A total of 170 individuals were enrolled for ocular examination; age was 51.0 ± 17.5 years; 52.9% were women; 100 had diabetes and systemic hypertension was present in 30. Systemic hypertension was present in 13 diabetic patients. Nine individuals did not wait for the pupil dilation at the consultation office, leaving before fundus documentation. Out of the 161 remaining individuals, 4 collaborated poorly with the examination procedure, mainly due to cultural barriers to understand the

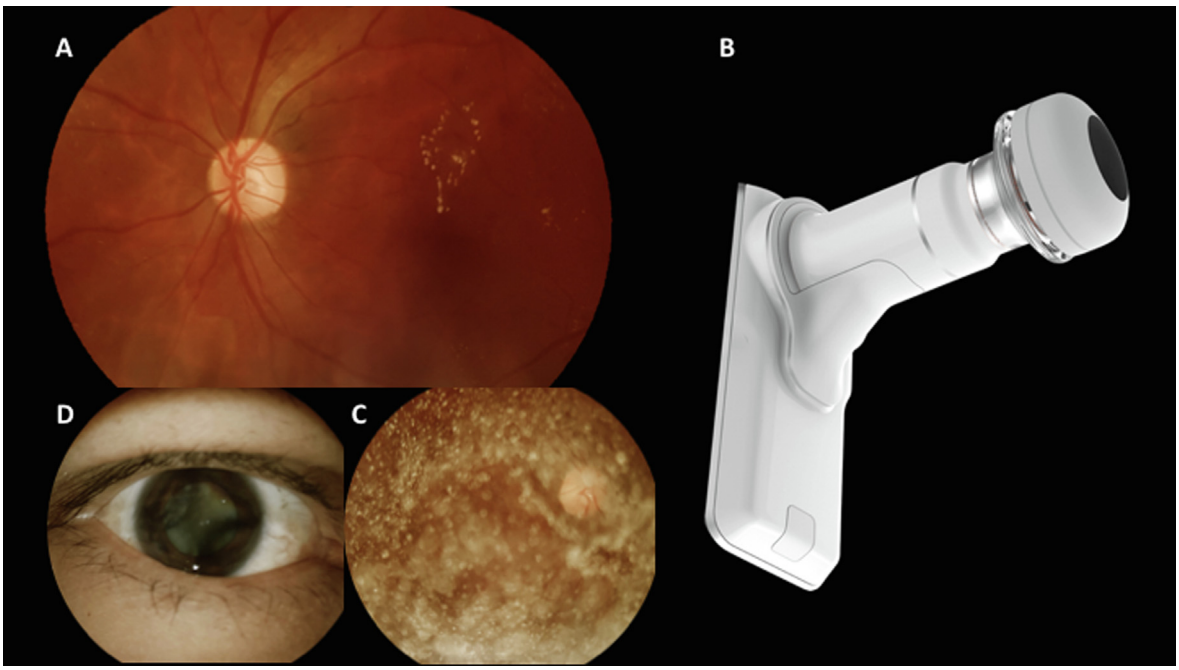

Fig. 1 – Ocular imaging of Xavante individuals with diabetes. Clockwise: (A) Merged retinal photographs of the posterior pole and nasal retina of a patient with diabetes depicting hard exudates on the macular area; (B) Portable imaging device; (C) Fundus photographs depicting a case of asteroid hialosis; (D) Anterior segment image showing cataract.

examination, not yielding good quality images. Hence, the complete imaging protocol of both eyes was obtained for 157 individuals, 95 with diabetes (60.5%) and 62 without diabetes (39.5%). (Fig. 2) Cataract was present in at least one eye in 61 patients; being severe in at least one eye in 24 patients, whose average age was 60.9 ± 23.2 years. Eighteen patients had already undergone cataract extraction. Mean IOP (in mmHg) was 14.9 ± 2.3 (right eye) and 14.9 ± 2.1 (left eye).

Among the 95 individuals with diabetes who underwent the complete ocular imaging protocol, DR classification was possible in 72 patients (75.8%), while the remaining 23 (24.2%) yielded ungradable images due to media opacities that precluded DR evaluation in at least one eye. Any DR was detected in 16 individuals (22.2%), with the following distribution: 2 with mild non-proliferative DR (NPDR), 12 with moderate NPDR, 1 with severe NPDR, and 1 with proliferative DR. Six patients had signs of macular edema in at least one eye; as a result, STDR was present in 7 individuals (9.7% DM patients; 43.7% DR patients).

Overall, 153 out of 190 eyes of DM patients yielded DR classification (80.5%); 37 eyes were not gradable because of media opacities: severe cataract was present in 21 eyes (56.7%), asteroid hyalosis in 16 eyes (43.2%) (Fig. 1) and posterior capsule opacification in 2 eyes (5.4%).

Individuals with and without DM were compared regarding gender, age, presence in at least one eye of pterygium, severe cataract, asteroid hyalosis and previous cataract surgery; the only significant difference was gender, as 66.7% of the individuals with diabetes were women, compared to 35.7 of those without diabetes (p = 0.000). The mean age of those with severe cataract was not significantly different among the groups. A sub-analysis was performed for the group of DM patients; no association was found between

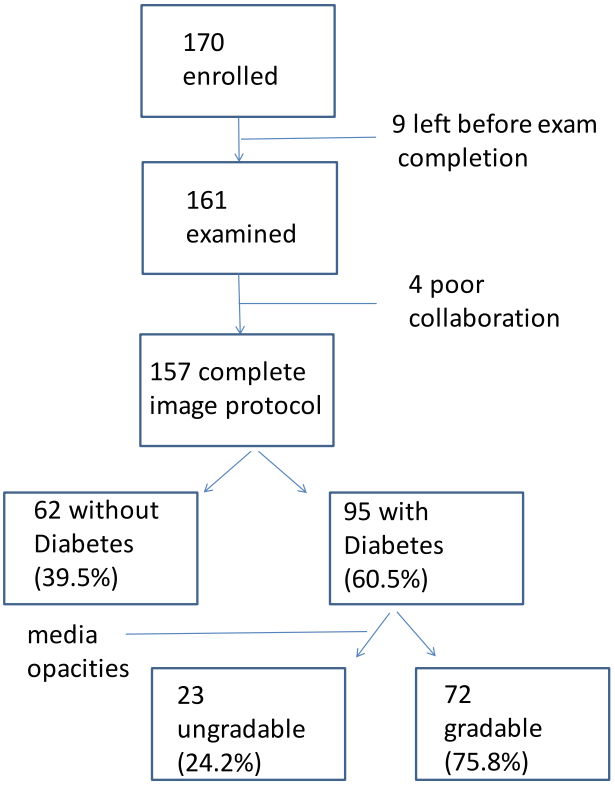

Fig. 2 – Number of enrolled and examined Xavante individuals.

STDR and age, systemic hypertension, DM diagnosis longer than 10 years.

4. Discussion

The main finding of the present study was that the screening of DR with a smartphone-based camera was feasible in the setting of a remote indigenous reserve in Brazil. Importantly, we also found that over 80% of fundus images were gradable, and the main reasons for ungradable images were media opacities such as cataracts and asteroid hyalosis, the latter found in an abnormally high frequency. In some cases, grading was not possible because of unfocused images or inadequate field of retinal image; in the absence of media opacities, these technical problems were mostly due to the poor collaboration of some patients, who sometimes did not understand the image acquisition routine because of cultural and language barriers.

In many remote areas of the world, including but not limited to indigenous reserves, diabetic patients face many barriers to an annual dilated eye examination [7,8]. In order to increase the rate of patients with diabetes who undergo annual eye examinations, new alternatives should be encouraged. There are already examples of DR screening programs with fundus photographs at indigenous reserves [9,10]; to the best of our knowledge, our results represent the first experience with South American indians. Retinal cameras and teleophthalmology allow patients to be assessed within their own remote communities, without the need for travel; a timely diagnosis and referral is of paramount importance in order to avoid diabetic blindness.

Mobile units have already been used for the screening of DR in indigenous populations elsewhere with favorable results, sometimes with traditional tabletop retinal cameras that travel inside trucks [11]; portable handheld devices have already been reported for the screening of indigenous populations in Australia [12]. In addition to the improved adherence to screening achieved with mobile units that use traditional retinal cameras, portable retinal cameras may allow increased coverage and lower cost to screening programs inside remote indigenous reserves, where the population is usually dispersed over various villages. Additionally, the success of a DR screening program based on retinal images is largely based on the quality of images. In our experience, the ungradability rate of 19.5% compares favorably with a recent experience in rural India of 34% [8].

In the present study, severe cataracts, besides preventing DR classification, were also the main ocular finding in patients who complained of visual impairment, overall and in DM patients as well. Even though some individuals had previously undergone cataract surgery in nearby cities, the high frequency of severe cataracts cases points to the low availability of specialized ocular care in this population, as is the case with other Brazilian regions. Cataract has been pointed as the main cause of visual impairment in Brazil and other Latin American countries [13]; increased ultraviolet exposure might explain its high prevalence in relatively young individuals from our sample [14]. Interestingly, the mean age of diabetic patients with severe cataracts was not different from non diabetic individuals with severe cataracts in our sample. Public health strategies to address the need for cataract surgery in underserved areas have been proposed, such as routine cataract surgeries in local hospitals or itinerary teams composed of operating ophthalmologists. [13] Pterygium, alongside with cataracts, is also related to ultraviolet light exposure, and has also been found to be highly prevalent in other Brazilian Indians [15].

In agreement with previous studies, DM was found to be more prevalent in woman at Xavante Reserves of Sandradouro/Volta Grande and São Marcos [4]. Previously, a 19.3% prevalence of DR at those reserves was reported. In the present study, a slightly higher prevalence of DR was found, 22.2%. This increase may have been due to the higher sensitivity of fundus photographs compared to indirect ophthalmoscopy [3], or because of the period that elapsed between the present exam and the previous one; additionally, the samples examined in the two occasions were not identical, which could explain the difference found in the prevalence rates. Nevertheless, the prevalence of DR could still be considered low, considering the poor glycemic control of that population [2]. Also, it should be considered the relatively short duration of the disease in this population, since DM was first reported in the Xavante Indians in 1996 [16], and this has been pointed as a possible reason for a lower rate of DR [2]. Other possible reason for a decreased prevalence of DR lies in high mortality rates among the Xavante [17] at younger ages, that presents a life expectancy as low as 61.7 years, lower than the Brazilian average [18]. Studies that evaluate the burden of diabetes mellitus point to a higher contribution of mortality in underserved areas, in opposition to a higher contribution of morbidity in the burden when the economic and sanitary conditions are improved [19]. Finally, certain genetic variants are hypothesized to play a role in a possible protection against DR progression [20].

All individuals with STDR or severe cataracts were referred to tertiary health care centers for specialized treatment, according to the framework of the Brazilian Indigenous Health subsystem [21]. The treatment of DR often has to be tailored to the individual clinical presentation and also to the healthcare environment. Interestingly, in a treatment cohort of predominantly indigenous Australians living in a remote and low-resourced setting, laser treatment was found to be viable and to preserve functional vision in the majority of patients, being an alternative to the pharmacological treatment, since the logistic burden and barriers to follow up can preclude frequent examinations and regular administration of intravitreal injections [22].

The strength of the present study resides in the successful experience of eye fundus documentation of Xavante, an indigenous population that is exposed to an epidemic of DM, with a novel portable retina camera. We hope that our results can put forward a telemedicine strategy for DR screening in such populations. In addition, by examining non-diabetic individuals, we could compare ophthalmologic findings such as cataracts among the groups.

There are limitations to this study. A major limitation was the short time that we had to conduct the examination and the use of a convenience sample, composed only of inhabitants from the larger villages. The small number of cases of STDR (n = 7) reduced the power to detect associations. Other microvascular diabetic complications were not analyzed, and

there was no visual acuity recording. Finally, macular edema diagnosis is ideally made with stereoscopic photographs or optical coherence tomography, none of which were used.

In conclusion, we showed that smartphone based retinal photography is a feasible and telemedicine-compatible strategy for DR screening in Xavante Indians. We believe that such a model could improve the ocular care of this underserved population. The high prevalence of severe cataracts in both diabetic and non-diabetic groups of this population is an alert for health care providers, calling attention for the necessity of more actions to improve cataract surgery availability for this ethnic group.

Declaration of Competing Interest

None.

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Author contributions

FKM: concept and design, collection of data, analysis of data, interpretation of data, preparation of manuscript.

ALDF: concept and design, collection of data, interpretation of data, preparation of manuscript.

JPBVF: concept and design, interpretation of data, preparation of manuscript.

LJF: concept and design, collection of data, interpretation of data, preparation of manuscript.

All authors contributed to critically revise the manuscript and have given final approval of the version to be published.

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