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# Relationship between Cataract and Metabolic Syndrome among African Type 2 Diabetics

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#### Abstract

**Objectives:** This study was performed to evaluate the prevalence and risk diabetics factors of cataracts in type 2 diabetics. The association between advanced diabetic retinopathy, vision loss and cataracts was also investigated among patients with diabetic retinopathy.

**Methods:** This was a community-based and analytic cross-sectional survey among 300 patients (males: 113, mean age:  $58 \pm 12$  years).

**Results:** One hundred forty patients (46.7%) had cataracts versus 95 patients (32%) with diabetic retinopathy (82 non proliferative and 13 proliferative).

Male sex, maculopathy, smoking, total and abdominal obesity, aging, uncontrolled diabetes, longer duration and high socioeconomic status were the univariate risk factors of cataracts. Only total obesity was the strong, significant and independent determinant of cataracts. There was a significant association between cataracts and blindness in the total study population. Among patients with diabetic retinopathy, those with proliferative diabetic retinopathy were older and presented higher frequency of metabolic syndrome, blindness, visual impairment and cataracts than their counterparts with non proliferative diabetic retinopathy. In patients with diabetic retinopathy, only aging, total obesity, cataract, and smoking were individually and significantly associated with visual impairment.

**Conclusion:** The prevalence of cataracts among these African type 2 diabetics was 46.7%. Total obesity was a strong independent determinant of the presence of cataracts. The removal of total obesity will contribute to prevent the risk of blindness due to cataracts among African type 2 diabetics.

**Keywords:** Cataracts; Aging; Metabolic syndrome; Smoking; Blindness; Africans; Type 2 diabetes

#### Introduction

Clinicians from developed and developing countries are facing a global epidemic of diabetes mellitus (DM), mainly type 2 diabetes (T2DM), driven by escalating rates of obesity and an increasing lifestyle changes such as physical inactivity, cigarette smoking, high fat intake, and excessive alcohol consumption, and low intake of fruits – vegetables. Currently, 171 to 246 million people worldwide are affected by diabetes, and this number is likely to increase to 360-380 million by 2025-2030 [1,2].

The burden of T2DM is driven by both macrovascular, microvascular (diabetic retinopathy), and blindness. Over the last twenty years (1988-2008), the causes of blindness have changed in proportion and actual number. Cataract has remained the major (39-67%) and number one cause of blindness globally, and nationally [3-7]. In West African type 2 diabetics, cataracts are more important cause of vision impairment than is diabetic retinopathy [5].

In general non African populations, DM, impaired fasting glucose, obesity, anti-hypertensive medication, metabolic syndrome, aging, smoking status, arterial hypertension, retinal vessel narrowing, undernutrition (lower body mass index), education, hypercholesterolemia, arthritis, deprivation exposure to low doses of ionizing radiation (X- rays to the face/neck) are known risk factors of the presence of cataract [8-18].

In West African diabetics, both T2MD, early onset of T2DM, and longer duration of diabetes were the most important determinants of cataracts [5].

Although the rates of obesity, DM blindness (12%) and visual impairment (27%), life style changes and cardiometabolic diseases constitute already a second burden of the disease [19-22] aside the traditional burden of endemic (malaria, tuberculosis) and pandemic (HIV/AIDS) infections in Democratic Republic of Congo (DRC). This is due to improvements in nutrition, water supplies, sanitation, and measles immunisation coverages in these privileged urban people. In addition, because of the large number of aging diabetics in DRC, cataracts are likely to provoke a heavy public health burden. DM cases community data based on the magnitude, pathogenesis, and complications of cataracts are not yet available in our setting. This lack hampers the identification of preventable causes of cataract and blindness as well the development of efficient prevention and intervention programmes. The aims of this study were i) to determine the prevalence of cataract among African type 2 diabetics; ii) to investigate the relationship between metabolic syndrome or

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its components and the presence of cataract in these type 2 diabetes mellitus patients.

#### Materials and Methods

#### Design and setting

A cross-sectional, analytic and community-based survey of T2DM patients  $\geq 20$  years of age (n=3010) and managed by 24 Catholic primary care centres for DM in Kinshasa town, capital of DRC, was carried out in November 2004. Kinshasa, the largest city (7 Million inhabitants) enjoys a tropical climate and constitutes an Hinterland with 24 administrative districts. The Catholic health system has established a primary care centre for DM in each district of Kinshasa city. Figure 1 shows the flow chart of the study design. The study protocol was approved by the University of Kinshasa Medical Ethics Committee and the study was performed in full compliance with the Declaration of Helsinki II.

#### Patients and sampling

Expected proportion (P) of cataracts was  $\geq 0.40$  (5), total Width (W) of confidence Interval was 0.10, and the sample size read on table across P, W, and 95% confidence level was 369 patients arounded to 384 patients (16 patients per district). Sixteen T2DM patients were randomly selected from the list of each district using random digits. Verbal informed consent was obtained from eligible patients after explanation of the study nature and rationale/ significances. All patients who refused to participate in this study, the patients with type 1 diabetes mellitus, and patients who did not complete their comprehensive physical examination were excluded.

#### Data collection

The structured and standardized questionnaires used to obtain information during 30 minutes, were adapted from the Blessey study [23].

The questionnaires sought relevant information on age, sex, DM duration, family history of DM, treatment compliance, ethnicity (Kongo, Ngala, Luba, Swahili), cigarette smoking, alcohol intake and socioeconomic status. The questionnaires were tested in a pilot study with 20 patients prior to the main study. Based on their responses and the level of understanding of the questions administered during 30 minutes, some ambiguous or unclear questions were restructured or modified. The researchers interacted with each respondent.

Data were collected during a comprehensive physical examination including anthropometry, blood pressure, Eye examination, and blood laboratory tests.

Weight, height, and waist circumference (WC) were measured in a standardized fashion by trained, certified observers. Height was measured with a portable stadiometer and recorded to the closest 0.1 cm. WC was measured with a non stretchable tape measures to the nearest 0.1cm. Weight was measured with a Soehnle beam scale (Soenle-Waagen Gmbh Co, Murrhardt, Germany) to the nearest 0.1 Kg. All instruments were calibrated once weekly. Blood pressure including systolic blood pressure (SBP) and diastolic blood pressure (DBP), was measured from the right arm of the seated patient after 15 minutes with an electronic validated digital devices (OMRON M7, Intelli/Sense, Kyoto, Japan). Fasting (10-12 overnight fast) blood glucose (hexokinase-glucose-6-phosphate dehydrogenase reaction), triglycerides and HDL-cholesterol were measured on commercially kits (Biomerieux, Marcy l'Etoile, France) and a Hospitex autoanalyzer (Hospitex Diagnostic, Florence, Italy).

Eye examination of each participant included visual acuity measurement, ocular alignment and motility, pupil reactivity and function, visual fields, intraocular pressure, slit lamp examination of the cornea, iris, lens and vitreous, and dilated fundus examination. This fundus examination was detailed and performed at the best possible mydriasis, after dilating the pupils with tropicamide (1%) and phenylephrine (10%), using direct ophthalmoscopes. For refraction and visual acuity testing, patients'eyes were first refracted with the AO Reichert SR-IV Programmed Subjective Refractor (AO Reichert Scientific Instruments, Buffalo, NY, USA). This result was refined as necessary with the use of standard subjective refraction techniques. Retinoscopy and trial lenses were used to refract the eyes of patients who could not use the SR-IV. Visual acuity was measured at 4m with the use of the charts and light box described by Ferris et al. [24,25].Visual acuity was measured separately for each eye and was defined according to the lowest line on the chart for which the majority of letters were read correctly. Visual acuity was measured twice, first with the patient's typical distance correction (that is, eyeglasses or contact lenses, if any) and again with the full required distance correction as determined by the study refraction data. Best corrected visual acuity was defined as the visual acuity in the better eye with full distance correction. Due to limited resources, retinal photography was excluded as a diagnostic tool. The experience in sub - Saharan Africa demonstrates a better than 80% concurrence between clinical and photographic assessment of the presence and absence of lesion associated with diabetic retinopathy [5].

#### Definitions

Diagnosis of T2DM was based on criteria established by the American Diabetes Association Expert Committee [26]: exhibiting either a fasting plasma glucose concentration of  $\geq$  126 mg/dL (7.0 mmol/L) on more than one occasion, and / or pharmacological treatment of diabetes. Total obesity was defined by body mass index (weight in Kg / height in m<sup>2</sup>)  $\geq$  30 Kg/m<sup>2</sup> [27]. Metabolic syndrome (Mets) was diagnosed according to the IDF criteria: WC  $\geq$  94 cm for men, WC  $\geq$  80 cm for women, triglycerides levels  $\geq$  1.7 mmol/L , HDL – Cholesterol < 1.03 mmol/L (male) or < 1.29 mmol/L (female), SBP  $\geq$  130 mmHg or DBP  $\geq$  85 mmHg, or treatment for lipid abnormalities, and fasting plasma glucose  $\geq$  100 mg/dL (5 mm/dL [28]. Arterial hypertension was defined as SBP  $\geq$  140 mmHg or DBP  $\geq$  90 mmHg or under antihypertensive drug treatment as recommended by the ISF / WHO guidelines committee [29].

Aging was defined as age  $\geq 60$  years. The Intake of  $\geq 4$  drinks/ day was considered as excessive alcohol intake. Smoking habits were classified into 2 groups: never smoker and current smoking  $\geq 1$ cigarette per day. Longer duration of diabetes was  $\geq 3$  years (median).

A diagnosis of diabetic retinopathy (DR) was made only where a patient had a minimum of one microaneurysm in any field, in addition to exhibiting haemorrhages (dot, blot, or flame shaped) and maculopathy (with or without clinically significant macula oedema). For the classification of DR, the modified Airlie House classification as introduced by the Early Treatment Diabetic Retinopathy Study (ETDRS) [30] was used as follows: non proliferative (NPDR), proliferative (PDR) and maculopathy. We defined dilated lens using Lens Opacities Classification System III grading as nuclear ( $\geq$  4), cortical ( $\geq$  2) and posterior subcapsular ( $\geq$  2) cataracts. Aphakic and pseudoaphakic eyes were included as operated cataracts for statistical analysis.

Blindness was defined by visual acuity <6/60 (TYPES III, IV and V of disability) using the World Health Organization definition and

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revision of classification [30]. Normal vision was defined by visual acuity between 1.0 and 0.3[6/6 - 6/18]. Uncontrolled diabetes was defined by fasting plasma glucose  $\geq 126$  mg/dL at evaluation.

#### Statistical analysis

Data were reported as proportions (%) for categorical variables and means  $\pm$  SD for continuous variables. The Chi-square test was used to compare proportions; comparisons of means between groups were performed using the Student t- test.

The univariate risk of cataracts (non operated + operated) was assessed in calculating Odds ratio (OR) with 95% confidence intervals (95% CI). Multivariate analysis such as logistic regression model, was used to assess the independent effect of selected variable on the presence of cataracts after adjusting for the effect of other potential confounders.

A P value < 0.05 was considered significant. Data analysis was carried out using the Statistical Package for Social Sciences (SPSS) for Windows version 13 (SPSS Inc, Chicago, IL, USA).

#### Results

A total of 300 T2DM patients (response rate of 78,1%) including 113 males (37,7%) and 187 females (62,3%) were examined. The mean age of the study population was  $58 \pm 12$  years (range 20-83 years). At the onset of diabetes mellitus, the mean age was  $51.9\pm12.8$  years. Mean duration of diabetes mellitus was  $6\pm7$  years with a median of 4 years (range 1 – 58 years). The duration of diabetes was very short: median of 3 years. Among these diabetics, 246 patients (82%) had uncontrolled diabetes.

#### **Cataracts prevalence**

The prevalence of any cataracts including operated eyes was 46,7% (n =140) whose 10% (n=14) operated, 30% (n=42) nuclear, 33% (n=46) cortical, and 27% (n= 38) posterior subcapsular cataracts. Thus cataracts were commoner than diabetic retinopathy (32% n=95) and maculopathy (10% n=31). Compared to T2DM patients without cataracts, T2DM patients with cataracts were older and had longer diabetes duration, and higher proportion of males, maculopathy, blindness, cigarette smokers , high socioeconomic status (SES), abdominal obesity and total obesity (Tables 1 and 2).

The risk of the presence of cataracts was multiplied by two times by males sex (in spite of the orverrepresentation of women), diabetes duration  $\geq$  3 years and cigarettes smoking, respectively. Cigarette

Variables of interest	Presence of cataract n = 140 Mean ± SD or n (%)	Absence of cataracts n=160 mean ± SD or n(%)	P
Age (years)	64 ± 9	53± 12	0.0001
Diabetes duration (years)	7 ±7	5±4	0.0007
Sex			
Males	65(57.5)	48(42.5)	0.002*
Females	75(40.1)	112(59.9)	
Age ≥ 60 years	102(68.9)	46(31.1)	<0.0001
Abdominal obesity	(65)	(39)	0.022
Total obesity	(62)	(38)	0.027*
Longer diabetes duration	86(56.2)	67(43.8)	0.0001
Maculopathy	24(77.4)	7(22.6)	<0.0001
Blindness	40(62.5)	24(37.5)	0.005
Cigarette smoking	29(63)	17(37)	0.012
High SES	99(51.6)	93(48.4)	0.016

\*significant findings

Table1: Variables associated with the presence of cataracts.

Variables of interest	O.R (95% CI)	P- value
Men vs. Women	2.02 (1.3 to 3.3)	0.005*
DM duration ≥3years vs. <3 years	2.2 (1.4 to 3.5)	< 0.001
otal obesity yes vs. no	1.3 (1.04 to 1.6)	0.027*
geing ≥ 60 years vs. < 60 years	6.7 (4.01 to 11.03)	< 0.001
moking Yes vs. no	2.2 (1.2 to 4.2)	0.024*
SES High vs. Low	1.3 (1.04 to 1.6)	0.024

Table 2: Univariate risk factors of cataract.

Variables	NPDR n=82 Mean ± SD or n(%)	PDR n=13 Mean ± SD or n(%)	Р
Age (years)	56.1± 12.6	62.2± 6.1	0.04*
DM duration (years)	8.6±7.5	11.2±8.1	0.246
Sex			
Men	29(35.4)	4(30.8)	0.746
Women	53(64.6)	9(69.2)	
Metabolic syndrome	21(25.6)	7(53.8)	0.038*
Blindness	3(3.7)	3(23.1)	0.007*
Visual impairment	17(20.7)	11(84.6)	0.0001*
Maculopathy	15(18.3)	5(38.5)	0.097
Cataract	39(47.6)	10(76.9)	0.049
Smoking	13(15.9)	4(30.8)	0.192
Alcohol intake	2(2.4)	0(0)	0.569

Table 3: Characteristics of cases of non proliferative diabetic retinopathy (NPDR) and cases of proliferative diabetic retinopathy (PDR).

Variables	Presence of visual impairment n = 29 Mean ± SD or n(%)	Absence of visual impairment n = 66 Mean ± SD or n(%)	Ρ
Age (years)	60.3± 11.8	50±12.1	< 0.001*
DM duration (years)	9.7± 7.2	8.7 ± 7.7	0.545
Sex			
Men	8(27.6)	25(37.9)	0.332
Women	21(72.4)	41(62.1)	
Family history of DM	27(93.1)	58(87.9)	0.445
Total obesity	10(34.5)	21(31.8)	0.447
High SES	8(27.6)	21(31.8)	0.680
Cataract	24(82.7)	25(37.7)	<0.01*
Smoking	9(31)	8(12.1)	0.027*

 Table 4: Characteristics of 95 patients with diabetic retinopathy stratified by the presence of visual impairment.

smoking conferred a 7- fold risk of cataracts, while 30% of excess of risk for cataracts were determined by both total obesity and high SES. The rest of variables were not associated with the presence of cataracts (results not shown). All patients with cataracts (100%) were defined by uncontrolled diabetes.

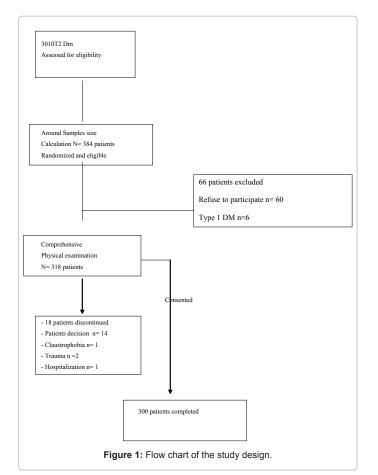
#### Multivariate analyses

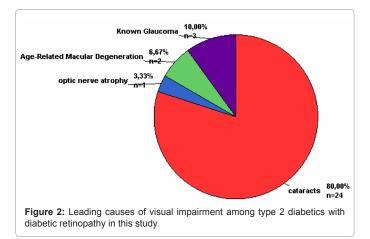
In logistic regression analysis adjusted for age, gender, diabetes duration, cigarette smoking and SES, only total obesity was significantly and independently associated with the presence of cataracts (Beta coefficient = 2.526, standard Error = 1.193, OR = 1.395% C, 1.01 - 1.4; P=0.034).

#### Types of diabetic retinopathy

Compared with T2DM patients with non proliferative diabetic

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retinopathy (NPDR), T2DM patients with proliferative diabetic retinopathy (PDR) were older (P< 0.05) and had higher proportions (P < 0.05) of metabolic syndrome, blindness, visual impairment and cataract (Table 3). In logistic regression and after adjustment for confounders, only cataracts were significantly and independently associated with PDR (OR = 3.395% CI 1.06 – 11. P= 0.049). In all T2DM with diabetic retinopathy, only aging, cataract, and cigarette smoking were significantly and individually associated with the presence of visual impairment (30% n = 29 /95) (Table 4). Among cases of visual impairment with diabetic retinopathy (n=29), 4/5 cases (n=24) had cataracts as leading cause of blindness (Figure 2).

#### Discussion

The present study showed that the prevalence of cataracts was unexpectedly high in these African type 2 diabetics. Cataracts were reported as a main cause of blindness and diabetic retinopathy. The influence of lifestyle changes and metabolic syndrome on cataracts and proliferative diabetic retinopathy formation was also evaluated in these African type 2 diabetics.

#### Female predominance in the study

The majority of the participants were females. From 1960, recurrent army conflicts have generated overrepresentation of women in the Congolese populations. Males may be underestimated as the study was carried out during the working day.

#### Prevalence of cataracts

The prevalence of cataracts was estimated 46, 7% among these black African type 2 diabetics. This rate is included within the interval of 39-67% cataracts reported in developed and developing countries [3-7]. This results confirms that cataracts remains the leading cause of the visual loss [3-7].

#### **Risk factors of cataracts**

Aging, male sex, longer duration of diabetes, high SES, cigarette smoking, abdominal obesity, and total obesity were individually associated with the presence of cataracts among these type 2 diabetics as reported elsewhere in Sub-Saharan Africa [8-18]. Male sex, uncontrolled diabetes and maculopathy (advanced diabetic retinopathy) were also significantly associated with the presence of cataracts among these type 2 diabetics. Epidemiologic studies from Europe have also identified long duration of diabetes disease, advanced age at the time of clinical diagnosis, advanced retinopathy and poor control of blood sugar level as risk factors for cataracts in diabetics [31-33]. As reported for diabetic Korean patients [34] the higher prevalence of diabetes mellitus was in females and most cases in this study and our previous studies [22,31,35] were also with a shorter duration of diabetes mellitus (median=3 years and 4 years).

A recent Korean study among type 2 diabetics showed that advanced age is not a risk factor of cataracts, but females are more common in the cataracts group than the control group [36].

US diabetic women are most likely to have cataracts than are female control [37]. However, the present study showed that the prevalence of diabetic cataracts was higher in males African type 2 diabetics than their female counterparts in spite of the overrepresentation of women.

Sub-Sahara African populations are experiencing sanitary transitions including epidemiologic transition (decrease in rates of non communicable diseases such as type 2 diabetes, hypertension, and obesity), demographic transition (aging), and nutrition transition (appropriate traditional African diet with low intake of salt, sugar, alcohol and fats replaced by Western fast food with low intake of fruits /vegetables and processed with refined sugar, low fibres, high salt and fats). Those sanitary transitions and lifestyle changes such as cigarette smoking, physical inactivity and stress explain the current double, triple or quadruple burden of the disease in Africa [19-21]. These findings may explain the significant high prevalence of cataracts among affluent diabetics (high SES), total obesity and abdominal obesity. The present study shows that there is fairly consistent evidence that cigarette smoking (nicotine) is related to the presence of cataracts as reported from Caucasian [37-39] and Chinese populations [40].

Although no significant association is noted between cigarette smoking and any particular type of cataract in a rural South Indian population, smokeless tobacco use is found to be significantly associated with nuclear cataract even after adjusting for age and sex [41]. It is well established that the very low sub-micromolar level of nicotine occurring in the tissues of smokers, induces endoplasmic reticulum (ER) stressors (cataractogenic stressors = Cata/Er stressors). The Cata/ ER stressors induces the unfolded protein response (UPR), which upregulates caspaces and produces reactive oxygen species (ROS) in lens epithelial cells (LECs). Thus, these caspases and the ROS lead to serious cellular damage, cell death, and cataract [42-46].

## Relation between visual acuity, metabolic syndrome, age, cataract, cigarette smoking and proliferative diabetic retinopathy

Among the present group with diabetic retinopathy (n=95 including 82 cases of NPDR and 13 cases of PDR), only aging, metabolic syndrome, blindness, visual impairment and cataract were significantly associated with the presence of proliferative DR. Moreover, only aging, cataract and cigarette smoking were significantly associated with the presence of visual impairment in these African type 2 diabetics. This is reasonable because cataracts are the main cause of visual loss (accumulation of reactive oxygen). Studies from literature report that the retinopathy is an influential factor on the degree of cataract [36,47-49]. Thus, the present data predict that many African type 2 diabetics will have cataracts and vision loss when their diabetic retinopathy has progressed. Diabetic retinopathy is a vascular complication of diabetes which is strongly influenced by the degree of oxidative stress. Cigarette smoking, aging, and chronic hyperglycemia are risk factors of development of oxidative stress. In addition, PDR is an advanced stage of retinal vascular complication which should be correlated with high degree of oxidative stress.

In multiple regression analysis, we found that only total obesity was the only significant and independent determinant for diabetic cataracts after adjusting for confounding risk factors. The relationship between obesity and cataracts has been investigated in many epidemiological studies, but the findings are not universally consistent. Higher body mass index (BMI) (total obesity) and higher waist to Hip ratio (abdominal obesity) are associated with the presence or incidence of cataracts [37,50-51].

Lower BMI is also associated with cataracts after adjusting for age, sex and other factors [53,54]. Several pathophysiological mechanism have been proposed to explain the association of obesity and cataracts. One theory suggests that leptin, a 16-kD pleiotopic cytokine expressed and secreted mainly by adipocytes [55], is involved in the molecular mechanisms underlying cataract formation [56]. Leptin increases accumulation of reactive oxygen species (oxidative stress) in various cellular models [57]. Indeed hyperleptinemia and leptin resistance [58], systemic oxidative stress [59] and inflammation [60,61] are significantly associated with total obesity. In addition, oxidative stress [62] and inflammation markers [60] may play a pathogenic role in cataract formation. Other data found no association between lower BMI and age-related cataract [62].

#### Clinical and public health implications

The present study supports the hypothesis of Shinohara et al. [63] which states that a cataract can be considered a window that can indicate the presence of systemic disorders such as metabolic syndrome, diabetes mellitus, severe diarrhea, dehydration, vitamin deficiency, Page 5 of 7

viral infections, hypertension, dyslipidemia, heavy metals intoxication, Alzheimer's disease, Parkinson's disease, and insulin resistance.

This is important for health practitioners because cataract is easily detected during a routine ocular examination. Earlier detection of systemic disorders can save the lives of patients. For Public Health perspectives, cataractogenic stressors (smoking, excessive alcohol intake, obesity, metabolic syndrome) from patients with cataracts should be the one of the first steps for the prevention and treatment of advanced diabetic retinopathy, vision loss, and systemic disorders. The control of hyperglycemia should be the second step for prevention of cataracts

#### Limitations

The present study is limited to demonstrate causality because of cross-sectional design. Prospective studies are recommended. It was not possible to demonstrate whether weight loss reduces the risk of cataracts. The limited resources in the study setting did not allow indirect ophthalmoscopy, systematic tonometry and the measurement of blood levels of lipids, C-reactive protein, fibrinogen, HbA1c, and oxidative stress markers.

#### Conclusion

Cataracts remain a leading cause of vision loss in these African type 2 diabetics. Presence of cataract was significantly associated with uncontrolled diabetes, male sex, longer duration of diabetes, abdominal obesity, total obesity, cigarette smoking advanced retinopathy and high socioeconomic status. The removal of total obesity, the strong independent determinant of the presence of cataracts, and cigarette smoking in type 2 diabetics will contribute to present risk of blindness related to diabetes. All diabetics with cataract should need comprehensive medical and eyes examinations.

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