·Clinical Research·

Role of Mediterranean diet, tropical vegetables rich in antioxidants, and sunlight exposure in blindness, cataract and glaucoma among African type 2 diabetics

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Abstract

• AIM: To assess whether regular Mediterranean diet and regular intake of vegetables may reduce the risk of blindness, cataract, and glaucoma in these type 2 diabetics.

• METHODS: A cross-sectional design was carried out among known black diabetics admitted at the diabetic clinics of Kinshasa, between October 2008 and March 2009. The Mediterranean-style dietary score (MSDPS) was used to characterize a Mediterranean-style dietary pattern in the study population using the Harvard semi quantitative FFQ adapted for Africa.

• RESULTS: Five hundred Type 2 diabetic patients were included in this study (48% of males; 40% aged ≥ 60 years). There was a significant association between blindness, cataract and aging; between blindness ($P<0.05$), cataract ($P<0.05$), glaucoma ($P<0.05$), and physical inactivity; between blindness ($P<0.05$), cataract ($P<0.0001$), glaucoma ($P<0.01$) and high SES, and a very significant association between blindness ($P<0.0001$), cataract ($P<0.0001$), glaucoma ($P<0.0001$) and exposure to sunlight. There was also a significant association between blindness, glaucoma, and male sex. Regular intake of Mediterranean diet, Brassica Rapa, beans, Abelmoschus, Musa acuminata reduced significantly the risk of blindness, cataract and glaucoma.

• CONCLUSION: Regular intake of Mediterranean diet, Brassica Rapa, beans, Abelmoschus, and Musa acuminata may significantly reduce the risk of blindness or its major causes among type 2 diabetes mellitus in Africa.

• KEYWORDS: type 2 diabetes mellitus; Mediterranean diet; blindness; cataract; Africa
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INTRODUCTION

The prevalence and incidence of diabetes mellitus (DM) and type 2 diabetes (T2DM) are increasing in sub-Saharan Africa, mostly due to Westernization and lifestyle changes resulting in reduced physical activity, metabolic syndrome (MetS), nutrition transition and subsequent obesity [1-3]. The same nutrition transition (rare intake of fruits and vegetables, but high intake of salt, fat and refined cereals), aging, urbanization and physical inactivity are incriminated in the increase of the prevalence of the MetS in developing countries [4].

Loss of glucose homeostasis defines DM as a syndrome. It is well known that DM is a progressive disease and is associated with high risk of atherosclerosis, kidney and nerve damage as well as blindness. Abnormalities in the regulation of peroxide and transition metal metabolism are postulated to result in establishment of the disease as well as its longer term complications. DM is associated with oxidative reactions, particularly those which are catalyzed by decompartmentalized transition metals, but their causative significance in diabetic tissue damage remains to be established [5]. Blindness is a severe vision impairment, not correctable by standard glasses, contact lenses, medicine, or surgery. The major blindness causes are cataracts, age-related macular degeneration, diabetic retinopathy, and glaucoma [6]. Eyes are the organs mostly exposed to environmental oxidative stress (sun light, ultraviolet rays). Aging, related to oxidative stress, is accompanied by the

increase in the prevalence of cataract, glaucoma, blindness and type 2 diabetes.

African-Americans, Hispanics, females, low socioeconomic status (LSES), and reactive oxygen species (ROS) are at higher risk of glaucoma [7]. Our previous study showed an increasing and a unexpected higher prevalence of blindness in central African diabetics (12%) than the prevalence from the literature [8]: the causes incriminated in this blindness are diabetic retinopathy (47%), cataract (33%), and glaucoma (19.8%).

The benefit of the Mediterranean-style dietary pattern in mitigating metabolic risk factors for T2DM and cardiovascular disease is well known [9]. In DM, oxidative stress due to chronic hyperglycemia, may result in overproduction of free-radical precursors and/or decreased efficiency of the antioxidant system[10-12].

Fruits and vegetables contain a vast array of antioxidant components, mainly polyphenols and flavonoids such as anthocyanins [13,14]. Flavonoids possess several physiological properties: antioxidant, antibacterial, antiviral, anti-inflammatory, anti mutagenic and antitumor activity, as well as the activation or inactivation of certain enzymes [15]. The researchers found that several flavonoids can prevent cell death at low concentrations; other flavonoids have limited or no effect. Quercetin, a flavonoid present at higher concentrations in yellow onions, prevents oxidative stress-induced cell death in retinal pigmentary epithelium (RPE) cells and has no cellular toxicity over a wide range of concentrations.

Dietary antioxidants prevent cataract formation by preventing oxidation of proteins or lipids within the lens in general and during aging also related to oxidative stress and cataract genesis[16, 17].

There are Congolese (Central Africa) data on association between low intake of fruits and vegetables with higher risk of DM [1,2,18], Diabetic Retinopathy, and blindness [19]. However, there is no evidence-based information pertaining to Mediterranean Diet, vegetables rich in antioxidants, and higher risk of blindness and its major causes such as glaucoma and cataract. To address this challenge, the present study was initiated.

The main objective of this study was to determine the frequencies of regular Mediterranean Diet and regular intake of leafy-fruit vegetables rich in antioxidants among Central African type 2 Diabetics. The second objective of the study was to assess whether regular Mediterranean Diet and regular intake of leafy-fruit vegetables rich in antioxidants may reduce the risk of blindness, cataract, and glaucoma in these type 2 diabetics. The effects of gender, aging, lifestyle changes and exposure to sun light on the higher risk of blindness, mature/immature cataract and glaucoma were also assessed among these type 2 diabetics.

Figure 1 Green leafy vegetables A:Cassava leaves (Pondu); B: Brassica rapa (Pointe noire).

Figure 2 Phaseolus vulgaris (Beans).

MATERIALS AND METHODS

Materials The survey was a cross-sectional and comparative design carried out among known and black diabetics consecutively admitted at the diabetic clinics of the General Hospital and the Salvation Army Boyambi Medical Center of Kinshasa, between October 2008 and March 2009. After informed and verbal consent of patients, examination methods included interviewer-administered structured and standardized questionnaire and measurements of weight and height. Questionnaire elicited information on age, gender, profession, ethnicity, sun light exposure, residence, education attainment, rural-urban migration and personal history of cataract surgery extraction. The study protocol was approved by the local Ethics Committees of the settings and conducted according to the principles of Helsinki II Declaration.

Study population Only type 2 diabetics with ophthalmologic examination data were included for the analysis. The rates of ocular diseases in patients who never consumed vegetables were compared with those of patients defined by regular intake of Mediterranean diet including red wine (antioxidants) moderate intake, and other leafy vegetables rich in antioxidants (Figure 1) and fruit-vegetables rich in antioxidants such as Phaseolus vulgaris (red beans) (Figure 2), Abelmoschus spp (Gombo) (Figure 3), and Musa acuminata (Plantains, banana big) (Figure 4), respectively.

Figure 3 Abelmoschus spp/okras (Gombo or dongo dongo).

Figure 4 Musa acuminate (plantain).

Methods

Dietary assessment To assess dietary intake, types of vegetables-frequency qualitative questionnaires were used. We also used a semi quantitative food-frequency questionnaire adapted from World Health Organization Stepwise approach [1]. The participants were asked about the average frequency of consumption of a given standard unit or portion size (basting spoon) for each type of vegetables during the previous days as well the number of days per week they had consumed that amount. There were 5 possible responses: "never", "rare" and "regular" consumption, median portion/day and median number of days/week for each type of vegetables intake. The list of leafy vegetables included Brassica rapa (Pointe noire). The list of fruit vegetables legumes included Phaseolus vulgaris (Beans), Musa acuminata (plantain), and Abelmoschus spp/okras (Gombo).

The Mediterranean-style dietary score (MSDPS) was used to characterize a Mediterranean-style dietary pattern in the study population using the Harvard semi quantitative FFQ adapted for Africa [20]; red beans containing the highest antioxidant capacity[9].

Ophthalmologic examination Eye examination included measurement of visual acuity, slit lamp examination, direct and/or indirect funduscopy, and tonometry by applanation. The World Health Organization criteria and the recommendation for revision were used to define blindness[21,22].

Definitions Legal blindness was defined as vision with best correction in the better eye worse than or equal to 20/20 or a visual field of less than 20 degrees in diameter [21,22]. Dense lens detected on slit lamp examination was diagnosed cataract (both mature and immature types). Primary Open glaucoma (POAG) was defined by chronic elevated intraocular pressure >21mmHg, associated to disturbance of the structure or functional integrity of the optic nerve characterized by atrophic changes (Disc cupping) with or without specific visual field defects[23].

As activity/diet in the central Africa region is totally different from that in Western cultures, standardisation was necessary to make our data comparable with those reported elsewhere. Physical activity assessment focussed on activities during work and leisure times: light (level 1) to moderate (level 2) activities without increase in respiratory frequency and heart rhythm (self-reported sedentary behaviour) of WHO/GPAQ (Global Physical Activity Questionnaire) using the Comparative Risk Assessment (CRA) methodology[24,25] versus intense activity with increase in respiratory frequency and heart rhythm (level 3). The validation of physical activity assessment was performed after Metabolic Equivalent of task (MET) transformation so that physical activity was defined by both the 75th percentiles of the seated and lying down position time (set) in hours and MET value range of 3-6 kcal/min. Physical activity was considered in patients with both SLTL 75th percentile and MET value range of 6-12 kcal/min.

Excessive alcohol intake, moderate intake and abstinence were defined by ⩾4 drinks/day for men, ⩾3 drinks/day for women, 1-3 drinks/day for men, 1-2 drinks/day for women and 0 drinks/day, respectively, according to WHO STEPwise approach (26). The level of SES (high for Tertile 3 and Tertile 2) and low for Tertile 1 was defined using a composite scale value scores [1] according to the stage of urbanization (westernisation, electricity, water supply, types of houses), income, and education level. The environment of residence in Kinshasa region was defined by 4 districts according to geographic site, the level of urbanization, socioeconomic status (SES) and population size : Lukunga, Funa and Mont-Amba as affluent and urban North-West districts versus Tshangu as semi-rural (slums) crowding (over 4 million/6 million people of Kinshasa) poor South-East district.

Aging was defined in patients with age ⩾50 years. Professions exposed to sun light were farmers and policy men controlling road traffic.

Statistical Analysis Data were expressed as proportions (%) for categorical variables. The Chi-square test was used to compare proportions. P<0.05 was considered significant. Data analysis was carried out using the Statistical Package

Table 1 Characteristics of the study population

Variables	*n*	%
Gender		
Men	240	48
Age ⩾60 years	200	40
Professions exposed to sun light	75	15
High SES	100	20
Physical inactivity	425	85
Diet		
Never consuming fruits	0	0
Never consuming vegetables	78	15.6
Antioxidants		
Mediterranean diet	33	6.6
Brassica rapa (choux pointe noire)	45	9
Phaseolus vulgaris (red beans)	62	12.4
Abelmoscus spp/Okras/Malvaceae(Gombo)	50	10
Musa acuminate (Plantain, banana big)	60	12
Blindness	69	13.8
Mature/immature cataract	36	7.2
Glaucoma	25	5

for Social Sciences (SPSS) for Windows version 15 (SPSS Inc, Chicago, IL, USA).

RESULTS

A total of 500 type 2 diabetics with overrepresentation of men were surveyed and examined. Their general characteristics are summarized on Table 1. Table 2 presents a significant association between blindness, cataract and aging; significant association between blindness, cataract, glaucoma and physical inactivity; significant association between blindness, cataract, glaucoma and high SES, and a very significant association between blindness, cataract, glaucoma and exposure to sunlight. There was a significant association between blindness, glaucoma and male sex, whereas sex did not significantly influence the prevalence of cataracts. Moreover, there was no significant association between glaucoma and aging.

Regular intake of Mediterranean diet, regular intake of Brassica Rapa, regular intake of Phaseolus vulgaris (beans), regular intake of Abelmoschus, and regular intake of musa acuminata reduced significantly the absolute risk of blindness, cataract and glaucoma, respectively (Table 3).

Table 2 Relationship between sociodemographic, lifestyle, sun light and ocular diseases *n* (%)

Explanatory variables	Blindness	m/i cataract	Glaucoma
Age group			
⩾60 years	60(30.0)	32(16.0)	11(5.5)
< 60 years	9(3.0)	4(1.3)	14(4.7)
Physical inactivity			
Yes	67(15.8)	34(8.0)	24(5.7)
No	2(2.7)	2(2.7)	1(1.3)
	P<0.05	*P*<0.05	*P*<0.05
Gender			
Men	49(20.4)	19(7.9)	20(8.3)
Women	20(7.7)	17(6.5)	5(1.9)
	P<0.00001	*P*<0.624	*P*<0.01
SES			
High	41(41.0)	32(32.0)	21(21.0)
Low	28 (7.0)	4 (1.0)	4(1.0)
	P<0.05	*P*<0.0001	*P*<0.01
Professions exposed to sun light			
Yes	61(81.3)	30(40.0)	20(26.7)
No	8 (2)	6(1.4)	5(1.2)
	P<0.0001	*P*<0.0001	*P*<0.0001

Table 3 Relationship between ocular diseases and dietary patterns *n* (%)

Explanatory Variables	Blindness	*m/i* cataract	Glaucoma
Mediterranean diet			
Regular intake	9(27.3)	3(9.1)	1(3.0)
Never vegetables intake	60(76.9)	33(42.3)	24(30.8)
	P<0.0001	*P*<0.005	*P*<0.001
Brassica rapa			
Regular intake	15(33.3)	4(8.9)	2(4.4)
Never vegetables intake	54(69.2)	32(41.0)	23(29.5)
	P<0.01	*P*<0.05	*P*<0.01
Phaseolus vulgaris			
Regular intake	18(29.0)	3(4.8)	4(6.5)
Never vegetables intake	61(78.2)	33(42.3)	21(26.9)
	P<0.0001	*P*<0.001	*P*<0.05
Abelmoscus spp			
Regular intake	9(18.0)	2(4.0)	1(2.0)
Never vegetables intake	60(76.9)	34(43.6)	24(30.8)
	P<0.0001	*P*<0.0001	*P*<0.05
Musa acuminata			
Regular intake	10(16.7)	5(8.3)	3(5.0)
Never vegetables intake	59(76.6)	31(39.7)	22(28.2)
	P<0.0001	*P*<0.01	*P*<0.05

DISCUSSION

The present study showed that regular Mediterranean Diet as well as regular intake of vegetables reduced the risk of blindness, cataract, and glaucoma in these type 2 diabetics. These findings highlighted a very low rate of consumption of vegetables in Africa [27]. Indeed, fruits are only eaten by children in general and diabetics are always discouraged to eat fruits by popular believes.

The present study is, to our knowledge, the first survey focussed on the effects of Mediterranean diet among African type 2 diabetics. The protection against chronic diabetes complications such as cataract, blindness, and glaucoma observed in this study may be explained by the significant reduction in cellular lipids level, and LDL oxidation (oxidative stress) reported by many researchers on Mediterranean diet [9,28]. This protective action has also been attributed to the higher level in antioxidants in Mediterranean diet [29, 30]. The antioxidant capacity from olive oil, flavonoids, fruits, vegetables, and red wine, the main components of Mediterranean diet [9,13,14,20] are supposed to counter the pro-oxidant of aging, age-related ocular diseases

(age-related macular degeneration, diabetic retinopathy, glaucoma, cataract). Indeed, the pathogenetic mechanisms in this diabetic eye complication are the deficiency of antioxidant system, and the chronic hyperglycaemia-related overproduction of free radicals precursors [10-12]. The antioxidant effects of the Mediterranean diet have also been reported to prevent atherosclerosis [30], cancer, and other mortalities.

The other significant protective factors against blindness, cataract, and glaucoma were regular intake of Brassica rapa (pointe noire), Phaseolus vulgaris (dry beans), Abelmoschus esculentus (gombo), and Musa acuminata (plantains). Brassica rapa is rich in polysaccharides (BRP1-1, BRPé-1, BRP3-1) which are known with a novel potential anti-hypoxia agent [31]. The antiradical activity of dry beans (Phaseolus vulgaris) is well known [32]. Dry beans considered to have the highest total antioxidant capacity [33-37] were recently identified as significant and independent protective factor against Metabolic syndrome (MetS) in African type 2 diabetics [27]. Abelmoschus esculentus Moench (gombo), often eaten in the North of Nigeria is characterized by antioxidant activities [38]. The ferric-reducing antioxidant power FRAP), and oxygen radical absorbance capacity (ORAC), markers of antioxidant capacity are reported in different varieties of Musa acuminata[39].

However, despite the intake of antioxidants from Mediterranean diet and locally grown vegetables, aging, usually inducing oxidative stress, was identified as a significant risk factor of both blindness and cataract among these diabetics.

Physical inactivity accompanied by a low grade inflammatory status was identified as a significant risk factor of blindness, cataract, and glaucoma. And a very significant association was shown between blindness, cataract, glaucoma, and exposure to sunlight by professions. Those results confirm the role of environmental factors in inducing the DNA damage, heart shock, apoptosis and oxidative stress. Indeed, after rural-urban migration, these type 2 diabetics are exposed to epidemiologic, demographic, and nutrition transition, with subsequent consequences such as obesity, inappropriate diet (high salt, fat, sugar, cigarette, and alcohol consumption) [40-44].

In general, primary metabolites of plants rich in antioxidants (carbohydrates, proteins, amino acids, lipids) are essential for cells survival and propagation [45]. The secondary metabolites from plants function in defence against predators and abiotic stresses like UV sunlight.

Indeed, we know that free radical-driven, molecular and cellular processes modulated by phenylpropanoid (antioxidants) in human cells cultures *in vitro* and in the *in vivo* animal models of tumours, inflammation, and cellular damage are reported in the literature [45-46].

These findings have several strengths such as new insights on oxidative stress and ocular diabetic complications that may lead to a casual antioxidant therapy [47] and health promotion. Thus, exercise, smoking cessation, moderate alcohol intake, and protection against sunlight are the background to curve the rising epidemic of type 2 diabetes and ocular complications in these Africans.

Health professionals could educate African diabetics in general and African male diabetics in particular, and prescribe them supplements rich in antioxidants [48] in terms of primary prevention. Globally, and in sub-Saharan Africa, after adjusting for age, the female sex is significantly associated with blindness and major causes of blindness because of low coverage and poverty [49-51]. In the present study and in other African studies [1,2,8,18,41,52-56], the diabetic African men are more susceptible to blindness and glaucoma and their causes such as hypertension, diabetic retinopathy, cataracts, cigarette smoking, low intake of vegetables-fruits, overrepresentation in hospital series because of income, and late admissions.

In the poor African context, both men and women with blindness lack awareness of the potential to cure these conditions, lack access to services, or do not accept services for a variety of cultural and social reasons. These issues prevent both women and men from availing the services they need but affect them differently [49]. The issue of late presentation has not improved over the last three decades[56].

The present study was limited because of its cross-sectional design which is not capable to demonstrate a casual association between the identified determinants and ocular diabetes complications. Indeed, only prospective studies can do that.

Endogenous markers of oxidative stress and antioxidants were not measured in blood samples. However, potential bias and confounding factors were reduced by the large size of participants and the use of the multivariate logistic regression.

In conclusion, both regular intake of the Mediterranean Diet and the consumption of locally grown vegetables including Brassica Rapa, dry beans, Abelmoschus esculentus, and Musa acuminata rich in antioxidants could exert significant protective effects on blindness, cataract, and glaucoma development in type 2 diabetics. Thus, the present data provide evidence to recommend supplement in antioxidants as useful tools against type 2 diabetes mellitus and its ocular complications. Aging, higher SES, male sex, physical inactivity, and exposure to sunlight were identified as risk factors of ocular diabetic complications.

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