Correlation between Glomerulopathy and Retinopathy in an African Population of Type 2 Diabetics

Michel Assane Ndour[1]*, Jean Pierre Diagne[2], Demba Diedhiou[1], Djiby Sow[1], Esperance Ciss[1], Ibrahima Mane Diallo[1], Muriel Diembou[1], El Hadj Fary Ka[3], Papa Amadou Ndiaye[2], Anna Sarr[1], Maimouna Ndour Mbaye[1]

[1]Department of Internal Medicine, Abass Ndao Hospital Center, Dakar, Sénégal
[2]Department of Ophtalmology, Abass Ndao Hospital Center, Dakar, Sénégal
[3]Department of Nephrology, Aristide Le DantecHospital Center, Dakar, Sénégal
Email: *michelassanendour@yahoo.fr

Abstract

Introduction: Diabetic microangiopathies are common, but their time to onset in a diabetic patient varies from subject to subject. The aim of our study was to study the correlation between renal and ophthalmic disorders in patients with type 2 diabetes. **Patients and methods:** This longitudinal, analytical study took place from March 1, 2018 to March 31, 2019 at the Abass Ndao University Hospital Center. It was studying retinal involvement in diabetic patients with glomerulopathy. **Results:** Of the 100 cases of diabetic glomerulopathy, they are divided into 70 women and 30 men with an average age of 58.2 years. The average duration of diabetes was 6.1 years and their average glycated hemoglobin (HbA1c) was 8.1%. Only 37% of patients had an HbA1c level below 7%. The other cardiovascular risk factors were high blood pressure (HBP) (39%), dyslipidemia (36%), and obesity (15%). Among these patients, diabetic retinopathy was present in 21% of the cases. Retinopathies were more frequent in the group of patients diagnosed with diabetes for less than 6 years (69%) and in patients with chronic renal disease with slightly reduced glomerular filtration rate (GFR) (34%). **Conclusion:** Our study allowed us to conclude that during the course of type 2 diabetes, the onset of chronic kidney disease does not systematically imply the presence of diabetic retinopathy. It is thus important to make screenings and assessments of systematic complications.

Keywords

Diabetic Retinopathy, Diabetic Nephropathy, Microangiopathy, Daka

1. Introduction

According to the latest estimates from the International Diabetes Federation (IDF), the total number of people with diabetes will increase from 415 million in 2017 to 628.6 million in 2045 [1]. In Senegal, the 2015 STEP survey reported an overall prevalence of diabetes of 2.1% [2]. Diabetes is a chronic disease, the severity of which remains linked to mainly vascular complications. However, microangiopathies (glomerulopathy, retinopathy and neuropathy) are more associated with type 1 diabetics compared to type 2 diabetic (T2D) patients.

Diabetic kidney disease is defined by a persistent elevation of urinary albumin excretion, and/or decreased glomerular filtration rate. It affects 15% to 30% of diabetics after 10 to 15 years of development [3]. It is one of the most common complications of diabetes and progresses to end-stage renal disease [4]. Eye complications of diabetes are dominated by diabetic retinopathy and macular edema. Diabetic retinopathy is the leading cause of blindness worldwide before the age of 50. In Africa, the prevalence of diabetic retinopathy is very variable. It is 18.3% in Tunisia [5] and 47.2% in Benin [6]. In Senegal, the prevalence is 60.8% according to a study carried out on diabetics of all types followed at the Abass Ndao hospital in Dakar [7].

In type 1 diabetics, the correlation between renal and retinal damage is well established [8]. In the latter, it is rather macroangiopathy and cardiovascular risk factors that determine the extent of microangiopathy.

In Senegal no study has been conducted in this direction. The aim of our work was to study the correlation between kidney and eye damage and associated factors in type 2 diabetic patients followed at the Abass Ndao University Hospital Center.

2. Patients and Methods

This is a longitudinal, descriptive and analytical study, conducted from March 1, 2018 to March 31, 2019. The study population consisted of type 2 diabetic patients followed at the Marc Sankale center and meeting the inclusion criteria. Free and informed consent was explained and then signed by the patient for inclusion in the study. We included in the study any type 2 diabetic patient with diabetic glomerulopathy. This glomerulopathy was confirmed twice by a 24-hour microalbuminuria higher than 30 mg/24h or a 24-hour proteinuria higher than 300 mg/24h. We excluded all other causes of nephropathy, type 1 diabetics and pregnant women, incomplete records, cases of major diabetes imbalance, cases of urinary tract infection, any patient who refused to participate in the study.

We have collected the following data:
- socio-demographic data: age (in years), gender,
- anthropometric data: body weight in kilograms, height in centimeters, body mass index (BMI, kg/m^2), blood pressure.
- the study of diabetes mellitus: the type, the age of the diabetes (in years), the

level of balance of diabetes by means of glycated hemoglobin (HbA1c). The balance of diabetes is judged according to the recommendations of the International Diabetes Federation [9].

We also assessed existing chronic complications:

- glomerulopathy: is the most frightening renal complication of type 1 and type 2 diabetes. It is classified into five evolutionary stages ranging from renal hypertrophy with glomerular hyper filtration to chronic renal failure with uremia [10];
- diabetic retinopathy: is the specific ocular complication of diabetes. Examination of the vitreous and fundus of the eye will make it possible to diagnose diabetic retinopathy and to specify the evolutionary stage. There are several classifications. We differentiate clinically and angiographically three stages (absence of diabetic retinopathy, non-proliferative diabetic retinopathy and proliferative diabetic retinopathy) subdivided into several groups [11];
- diabetic neuropathy: is a complex disease due to both damage to the nerve fibers and the micro-vessels associated with them. We distinguish several types of diabetic neuropathy: distal peripheral neuropathies; mono neuropathies; autonomic neuropathies [12].

The cardiovascular risk factors considered in this study were: high blood pressure (hypertension), dyslipidemia, physical inactivity, obesity, smoking, age, and diabetes. We also evaluated the current drug treatment.

The ophthalmological examination included: an analysis of visual symptoms, the evaluation of visual acuity, intraocular pressure (search for glaucoma), examination of the iris and lens (search for rubella and cataracts) and of the vitreous. Finally, the examination of the fundus of the eye was performed after pupillary dilation (eye drops at 1% tropicamide [Mydriaticum]) and Phenylephrine eye drops [Neosynephrine] 2.5% to 10% without exceeding 2 instillations) and only in the absence of cataract. It was done with a slit lamp, using an examination lens with or without corneal contact. It must be comprehensive and include careful analysis of the macular region, the papilla and the peripheral retina. It makes it possible to diagnose the existence of diabetic retinopathy and to specify its degree of severity.

The data were collected on a pre-established individual questionnaire which was addressed to the objectives of the study, in strict compliance with medical confidentiality. Other complementary examinations were carried out according to clinical orientation.

The results were captured and analyzed using an electronic questionnaire developed with SPSS 24.0 software. The graphs were made using the Excel module of the MS Office 2014 suite. We performed a comparative analysis of the different groups (with and without diabetic retinopathy) to assess the factors statistically correlated to the existence of retinopathy and its worsening, but also worsening of glomerulopathy. The difference was considered statistically significant for a $p < 0.05$. The Odds Ratio (OR) surrounded by its confidence interval was used to quantify the strength of the link. Variables with more than 10% missing

data were not analyzed.

3. Results

3.1. Patient Clinical Profile

During the study period, 100 type 2 diabetic patients with diabetic glomerulopathy were included. The patients were divided into 70 women and 30 men. The sex ratio Male/Female was 0.4. The average age of the patients was 58.2 years with a standard deviation of 10.4. Among women, the age group between 58-68 years was 38%. In men 50% were between 47 - 57 years old. The average age of the women was 57.4 years. The average course of diabetes was 6.1 years. Diabetes had progressed for less than 6 years in half of the patients. In the majority of patients, diabetes was discovered before a cardinal syndrome with an imbalance in pure hyperglycemia. The average blood sugar was 1.7 g/l (10.16 mm/l) with a standard deviation of 1.6 g/l. The average HbA1c was 8.1% with a standard deviation of 3.4. Diabetes was balanced in 37 patients with an HBA1c of less than 7% (Table 1).

3.2. Coexisting Complications

In our series, 23 patients were diagnosed with diabetic neuropathy, including 6 cases of neuroarthropathies, 13 cases of vegetative neuropathies (orthostatic hypotension, chronic constipation) and 3 cases of movement disorders.

3.3. Cardiovascular Risk Factors

They were:
- hypertension in 9 patients and 1 case of hypertensive retinopathy was found in these patients;
- a sedentary lifestyle in 15 patients, therefore 65%;
- smoking in 2 men;
- dyslipidemia in 9 patients;

Table 1. Clinical profile of patients.

Data	Frequency (%)
Effective	100 (100%)
Sex ratio M/F	0.4
Averageage	58.2 ± 10.4 years
Age classes	
Women	58 - 68 ans (38%)
Men	47 - 57 ans (50%)
Average duration of development of diabetes	6.1
Average blood sugar	1.7 ± 1.6 g/l
Average of HbA1c	8.1% ± 3.4%
HbA1c < 7%	37%

- moderate renal failure in 1 patient and severe in 6 patients;
- the prevalence of dyslipidemia was 36%. The increase in LDL cholesterol was the predominant lipid abnormality and was found in 19 patients (19%); the mean was 1.3 g/l with a standard deviation of 0.5 g/l. The extremes were 0.04 to 2.6 g/l;
- obesity in 15% of the patients were obese.

3.4. Correlation between Renal Involvement and Ophthalmic Involvement

Patients with diabetic retinopathy were divided into 7 men and 16 women, with an average age of 57 years. In patients with chronic kidney disease (CKD) with moderate GFR, 4 patients with minimal non-proliferative diabetic retinopathy (NPDR) are observed, 1 patient with mild NPDR and 1 patient with moderate NPDR are also observed. In patients with moderate CKD, there was only 1 case of minimal NPDR and 1 of moderate NPDR. Only one case of severe CKD associated with minimal NPDR was found (Figure 1). The profile of patients with retinopathy according to their cardiovascular risk and their chronic kidney disease has been settled in Table 2.

4. Discussion

This was a prospective, analytical longitudinal study on the correlation of renal and ophthalmological involvement in T2D patients followed at the Mark Sankale center. It took place from March 01, 2018 to March 01, 2019 in the Abass NDAO University Hospital Center respectively at medical clinic 2 and the ophthalmology department.

4.1. Epidemiological Characteristics

We had a female predominance (70%), with a sex ratio of 0.4. A similar result was found in Sweden (59%) by R. Eggertsen *et al.* [13], in 2009. While F. DJROLO
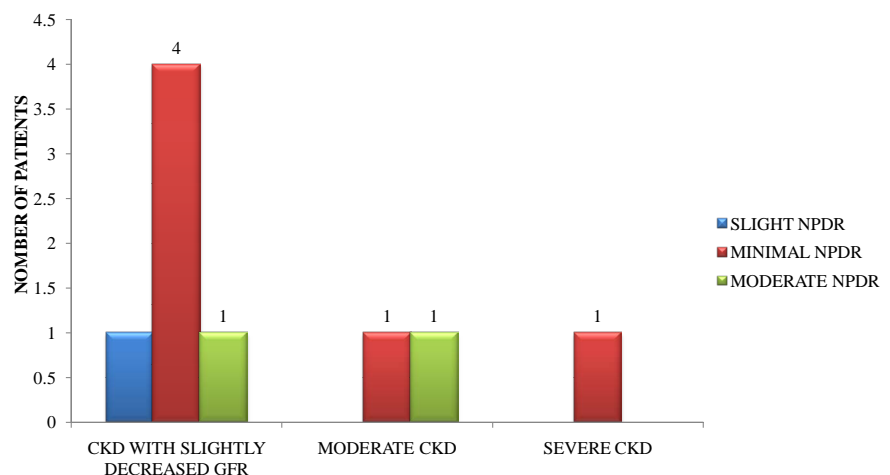

Figure 1. Cases of NPDR according to the stage of chronic kidney disease.

Table 2. Profile of patients with retinopathy according to their cardiovascular risk and their chronic kidney disease.

diabetic retinopathy	age	gender	seniority	ckd stages	hb1ac	microalb	hbp	tobacco	physical activity	dyslipidemia
minimal npdr	60	m	23	gfr slightly decreased	12.1	30	0	1	Moderate	1
minimal npdr + ischemic maculopathy	56	m	5	normal or increasing gfr	7.7	32	1	0	Sedentarity	0
moderate npdr + focal edematous maculopathy	53	f	3	normal or increasing gfr		36	0	0	Sedentarity	0
moderate npdr	37	f	1	normal or increasing gfr	9.5	62	0	0	Moderate	0
moderate npdr	54	f	4	normal or increasing gfr		36	0	0	Sedentarity	0
moderate npdr + cortical cataract	62	f	5	gfr slightly decreased	9.9	190	1	0	Sedentarity	0
moderate npdr + fedematous maculopathy	50	f	5	gfr slightly decreased	12.7	32	0	0	Slight	1
moderate npdr + evolutive cortico nuclear cataract	68	m	3	normal or increasing gfr	5.8	117	0	0	Moderate	1
moderate npdr + evolutive cortico nuclear cataract	61	f	5	moderate chronic renal failure	6.1	100	1	0	Moderate	0
moderate npdr	63	f	2	gfr slightly decreased	5.8	130	0	0	Sedentarity	0
moderate npdr	42	f	5	gfr slightly decreased	9	50	0	0	Moderate	0
moderate npdr	59	f	18	severe chronic renal failure		30	1	0	Sedentarity	1
severenpdr	57	f	1	moderate chronic renal failure	7.7	30	1	0	Sedentarity	0
severenpdr	70	m	19	normal or increasing gfr	9.1	36	1	0	Sedentarity	0
severenpdr + beginning cortical cataract	60	f	15	moderate chronic renal failure		125	0	0	Sedentarity	1
severe npdr	61	m	2	normal or increasing gfr	6.7	132	0	0	Sedentarity	0
severe npdr	58	m	3	gfr slightly decreased	6.2	62	0	1	Moderate	1
minimal pdr	54	f	1	normal or increasing gfr	10.5	36	0	0	Sedentarity	0
minimal pdr	45	f	10	gfr slightly decreased	11.2	300	1	0	Sedentarity	1
minimal pdr	67	f	15	moderate chronic renal failure	9.9	31	0	0	Moderate	0
moderate pdr + focal edematous maculopathy	54	f	4	gfr slightly decreased	6.6	122	1	0	Sedentarity	0
severe pdr	63	m	3	normal or increasing gfr	14.25	45	0	0	Sedentarity	1
severe pdr + hypertensive retinopathy	63	f	12	moderate chronic renal failure	5		1	0	Sedentarity	1

et al. [14] in their studies had found a predominance of men (66%). This strong female trend could be explained by the prevalence of diabetes among women.

The average age of our patients was 58.2 years with a standard deviation of 10.4 years. This average age can be superimposed on that found by F. DJROLO *et al.* (53 years) [14]. It is significantly lower than that reported in Europe (Swe-

den) by R. Eggertsen *et al.* [13] in 2009 in a study carried out on screening for retinopathy and microalbuminuria in patients with type 2 diabetes (mean age of 71 years old). The average age found in African countries, which is lower than that of certain studies conducted in Europe. This could be linked to the lower life expectancy in our regions.

4.2. Clinical Data

The average course of diabetes was 6 years. Diabetic patients had an evolving duration for less than 4 years.

Indeed, in a study conducted in Benin F. Djrolo *et al.* [14] found a duration of development of diabetes of 6 years. A longer course of diabetes is reported in the Swedish study by R. Eggertsen *et al.* [13] who found 8.1 years for men and 8 years for women. This could be explained by the late diagnosis. After 4 years of evolution of diabetes, patients already have diabetic nephropathy.

The average blood sugar was 1.7 g/l (10.16 mmol/l). The average HbA1c was 8.1%. This imbalance in glycemia and glycated hemoglobin is reported in both Africa and Europe. F. Djrolo *et al.* [14] found an average fasting blood glucose of 2.2 g/l. for Eggertsen *et al.* [13], the average fasting blood glucose of 9.2 mmol/l (1.65 g/l) in men and 9.6 mmol/l (1.72 g/l) in women.

This finding reflects the delay in systematic screening for diabetes in subjects at risk in our countries, in particular in families where one or more members are already known to have diabetes, thus justifying the presence of complications straight away.

It is necessary to screen for diabetic complications in our patients even in the event of a recent discovery.

4.3. Preexisting Complications

In our series, 23 patients had diabetic neuropathy, including 6 cases of neuroarthropathies, 13 cases of vegetative neuropathies and 3 motor disorders. The prevalence varies according to the diagnostic methods used (symptoms alone, symptoms and clinical signs, paraclinical examinations). According to M. Davies *et al.* in a study on the prevalence of neuropathy in T2D, more than a quarter of patients presented with nervous abnormalities at the time of diagnosis [15]. P J. Dyck *et al.* in their study on the prevalence by stages of severity of various types of diabetic neuropathy, retinopathy and nephropathy, estimate that around 50% of diabetic patients will develop peripheral neuropathy [16]. Diabetic nephropathy was 100%. Microalbuminuria was assayed in 96 patients and 24-hour proteinuria was assayed in 8 patients, all of which were above normal.

4.4. Correlation of Nephropathy and Retinopathy

In our study 21% of patients had diabetic retinopathy. F. Djrolo *et al.* [14] report a similar prevalence of 17%. Eggertsen *et al.* [13] in Sweden reported a significantly higher rate of 41.6%, however, in older patients. In all of these studies, less than 50% of patients with nephropathy had diabetic retinopathy, which suggests

that the presence of diabetic nephropathy was not systematically correlated with ophthalmic diabetes. Diabetic retinopathy was non-proliferative (NPDR) in 17% of cases (10 minimal cases, 2 mild cases, 5 moderate cases) and proliferative in 6% of patients (3 minimal cases, 1 moderate case, 2 severe cases). Eggertsen *et al.* [13] report a similar distribution with 37% NPDR and 4.3% of proliferative diabetic retinopathy (PDR). NPDR was more common in these studies, demonstrating the early development of nephropathy in these patients. This could be linked to the short course of diabetes in the study population, which was between 0 and 5 years in 68% of patients. Nine patients had maculopathy including 7 cases of focal edematous maculopathies and 2 cases of ischemic maculopathies. Edematous maculopathies were associated with 1 case of minimal NPDR, 1 case of moderate NPDR and 1 case of moderate proliferative diabetic retinopathy (PDR). One case of ischemic maculopathy was associated with minimal NPDR.

Five patients had hypertensive retinopathy out of 39 hypertensive patients. We can remember that the proteinuria cases observed in the absence of retinopathy are not due to high blood pressure.

In 46 patients, the ophthalmic examination was normal and in 78% of the patients there was no diabetic retinopathy at the back of the eye. In the Eggertsen *et al.* [13] series, diabetic retinopathy was absent in 58.4% of patients. F. Djrolo *et al.* [14] in their study in Benin reported an 83% higher rate of free patients.

However, the contribution of angiography and optical coherence tomography (OCT) is essential; this review could not be done due to its high cost. The clinical examination is also very limited to classify a diabetic retinopathy.

5. Conclusion

Our study on the correlation of diabetic renal disease and diabetic retinopathy, confronted with data from the literature, concluded that during the course of type 2 diabetes, despite the comparability of their etiopathogenic mechanisms and factors of common risks, the occurrence of one does not automatically imply the presence of the other. We cannot therefore formally affirm the existence of diabetic retinopathy on the basis of the presence of diabetic nephropathy. Given the seriousness of these two complications, one of which (nephropathy) is likely to jeopardize the vital prognosis and the others (retinopathy) which seriously compromise the quality of life of the patient, it remains essential that their research be performed independently and upon discovery of diabetes despite the often very limited resources of patients in developing countries.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] International Diabètes Fédération (2017) Atlas du diabète de la FID. 8ème Édition.

[2] Ministère de la santé et de l'action sociale MSAS (2015) Enquête nationale sur les facteurs des risques des maladies non transmissibles, STEP Sénégal, rapports préliminaires: Indicateurs clés. http://anads.ansd.sn/index.php/catalog/127

[3] Hannedouche, T. (2007) Néphropathie diabétique: Signes et diagnostic. Nephrohus Learning. http://www.nephrohus.org/ Visité le 12 Novembre 2015.

[4] Adler, A.L., Stratton, I.M., Neil, A.W., *et al.* (2000) Association of Systolic Blood Pressure with Macrovascular and Microvascular Complications of Type 2 Diabetes (UKPDS 36): Prospective Observational Study. *British Medical Journal*, **321**, 412-419. https://doi.org/10.1136/bmj.321.7258.412

[5] Ben Abdelaziz, A., Tlili, H., Drissi, L., Gaha, R., Knani, H. and Ghannem, H. (2004) Profil clinique des patients diabétiques suivis en première ligne (Sousse, Tunisie). *Revue d'Epidémiologie et de Santé Publique*, **52**, 113-122. https://doi.org/10.1016/S0398-7620(04)99310-8

[6] Djrolo, F., Houngbe, F., Attolou, V., Vode, A.G. and Vimadje, A.M. (1999) Rétinopathie diabétique: Quelques aspects épidémiologiques à Cotonou. *Louvain Médical*, **118**, 262-269.

[7] De Medeiros-Quenum, M., Ndiaye, P.A., Cissé, A., *et al.* (2003) Aspects épidémiologiques et angiofluorographiques de la rétinopathie diabétique au Sénégal. *Journal Français D'Ophtalmologie*, **26**, 160-163.

[8] Klein, R., Zinman, B., Gardiner, R., *et al.* (2005) The Relationship of Diabetic Retinopathy to Preclinical Diabetic Glomerulopathy Lesions in Type 1 Diabetic Patients. *Diabetes*, **54**, 527-533. https://doi.org/10.2337/diabetes.54.2.527

[9] Chraibi, A., Seqat, M. and Nejjari, C. (2015) Équilibre glycémique et satisfaction de patients diabétiques de type 2 insuffisamment contrôlés au Maroc: Résultats après 6 mois de traitement par insuline glargine. *Médecine des maladies Métaboliques*, **9**, 695-700. https://doi.org/10.1016/S1957-2557(15)30253-4

[10] Zanchi, A., Cherpillod, A., Pitteloud, N., *et al.* (2014) Insuffisance rénale et diabète, les précautions à prendre. *Forum Médical Suisse*, **14**, 100-104. https://doi.org/10.4414/fms.2014.01761

[11] Koki, G. and Bella, A.L. (2010) Rétinopathie diabétique du Noir africain: Etude angiographique. *Cahiers Santé*, **20**, 127-132. https://doi.org/10.1684/san.2010.0207

[12] Said, G. (1998) Les neuropathies diabétiques: Classification et prise en charge. *Diabetes & Metabolism*, **24**, 50-54.

[13] Eggertsen, R., Kalm, H. and BLohmé, G. (1993) The Value of Screening for Retinopathy and Microalbuminuria in Patients with Type 2 Diabetes in Primary Health Care. *Care*, **11**, 135-140. https://doi.org/10.3109/02813439308994916

[14] Djrolo, F., Doutetien, C. and Attolou, V. (2001) La microangiopathie diabétique étude de la concordance entre la rétinopathie et la néphropathie dans une population de diabétiques noirs africains à Cotonou (Bénin). *Louvain Médical*, **120**, 305-309.

[15] Davies, M., Brophy, S., Williams, R. and Taylor, A. (2006) The Prevalence, Severity, and Impact of Painful Diabetic Peripheral Neuropathy in Type 2 Diabetes. *Diabetes Care*, **29**, 15-18. https://doi.org/10.2337/dc05-2228

[16] Mulder, D.W., Lambert, E.H., Bastron, J.A. and Sprague, R.G. (1961) The Neuropathies Associated with Diabetes Mellitus. A Clinical and Electromyographic Study of 103 Unselected Diabetic Patients. *Neurology*, **11**, 275-284. https://doi.org/10.1097/00132985-196104000-00001