

Screening for Diabetic Nephropathy by Measuring Micro-Albuminuria on 24 Hour Urine

Thiam^{1,2*} S, A Ndiaye^{1,3}, I.Y Soumah¹, F Cissé^{1,2}, A Samba^{1,3}, N.F Coly⁵, F Diedhiou¹, H Agossou¹, A Ndiaye⁴, F Diallo^{1,3}, N.D SALL^{1,4}

¹Laboratory of Biochemistry, University Cheikh Anta DIOP of Dakar, Senegal

²Laboratory of Biochemistry, Dalal Jamm National Hospital, Guediawaye, Senegal

³Laboratory of Biochemistry, Aristide le Dantec National Hospital Center, Senegal

⁴Medical Analysis Laboratory, Abass Ndao, Senegal

⁵ UFR Health, University of Thies, Senegal

(Corresponding author) Souleymane THIAM

Abstract: *Micro-albuminuria is an early marker of diabetic nephropathy (DN) but also a predictor of morbidity and mortality. The aim of our work was to assess the frequency of DN by measuring micro-albuminuria (mA) on 24h urine. This was a retrospective study carried out in 2018 in 450 diabetic patients having undergone an mA assay in the multipurpose laboratory of the ABASS NDAO hospital, in Dakar, Senegal. The mA was assayed on 24h urine with the BTS-350 (Barcelona, Spain). The median age in our study population was 56.31 ± 12.75 years with a predominance of the 40-59 years age group (48%). We found a predominance of women (62%) with a sex ratio of 0.61. The prevalence of DN was 26% in the general population with a predominance in subjects aged over 60 (15.8%), female (16.9%) and in T2D (21.6%) with a statistically significant difference (p < 0.05). Proteinuria was found in 6% of patients (n = 27) with a predominance in women aged over 60 with type II diabetes. Diabetic nephropathy is a frequent complication of diabetes mellitus. Its prevention requires an early diagnosis by the dosage of micro-albuminuria. Its dosage should be popularized especially in subjects over 50 years to improve the quality of care.*

Keywords: Diabetes, Diabetic nephropathy, Micro-albuminuria, 24h urine

1. Introduction

Diabetes is a metabolic disorder characterized by the presence of hyperglycemia due to a reduction in insulin secretion or insulin action, or both [1]. It is increasing more and more in developing countries and has given rise to concern among international health institutions as a major public health problem [2]. Untreated diabetes can be accompanied by severely debilitating and degenerative complications such as macro-angiopathies and micro-angiopathies. One of the most serious micro-angiopathic complications is diabetic nephropathy [3, 4]. DN affects 15 to 30% of people with diabetes after 10 to 15 years of development [5]. In Senegal the national prevalence is not yet known, but hospital data show a prevalence ranging from 24% to 48.7% in type II diabetics [6, 7].

A silent and insidious development, ND affects the small vessels of the kidney glomeruli and could lead to chronic renal failure (CKD) if it is not treated early. This situation would require the initiation of a replacement therapy, access to which remains very limited due to its very high cost [8]. Therefore, it is compulsory to find an early marker of this complication to initiate preventive actions towards the mostly threatened subjects [9] but also an easy dosage parameter for laboratories with limited resources. Micro-albuminuria is a biomarker that could allow the early detection of manifestations of renal disease at an early and reversible stage in order to delay the progression of diabetic nephropathy [1]. This guided us in our project to assess the

prevalence of diabetic nephropathy by measuring microalbuminuria.

2. Materials and Method

This was a retrospective analytical study carried out at the Polyvalent laboratory of the Abass NDAO hospital (CHAN) from January 01 to June 30, 2018. Diabetics with a micro-albuminuria were included in our study. Data were collected from the laboratory registry considering age, gender and type of diabetes. Micro-albuminuria assay was carried out on 24h urine collected by the patient and sent to the laboratory the next morning to be measured and assayed the same day. The BTS 350 semi-automated system (Barcelona, Spain) was used for the dosage with Biosystem® reagents following the principle of turbidimetry with the formation of agglutinate between the albumin present in the urine and the latex particles covered with human anti-albumin antibodies. The diagnosis of diabetic nephropathy was retained if the micro-albuminuria was between 30 and 300 mg / 24h according to the recommendations of KDIGO [11]. The results were entered using Excel 2013 and analyzed with SPSS v.20 software. Comparison of the average micro-albuminuria was made using the Chi-square test. A value of p < 0.05 was considered significant in term of difference.

3. Results

Figure 1 depicts the distribution of the population by sex. A total of 450 requests for micro-albuminuria were identified. There was a female predominance with a sex ratio of 0.61.

The median age was 56.31 ± 12.75 years with extremes of 21 and 85 years. Most subjects were aged between 40 and 59, (48%) ($n = 216$) followed by subjects over 60 years 42% ($n = 189$). There was a clear predominance of type 2 diabetes compared to type 1 diabetes (70% vs. 30%) (Table I). Diabetic nephropathy was found in 117 patients, a prevalence of 26%. It was predominant in subjects aged over 60 (15.8%, $n = 71$), in type II diabetics (21.6%, $n = 97$). Six percent of patients, predominantly women were aged over 60 with type II diabetes who already had proteinuria at the time of dosing, (4%, $n = 18$) (Table II).

A significant variation in the median values of micro-albuminuria was found in women and subjects aged over 60. No significant difference was found based on the type of diabetes. The bivariate and multivariate analyzes found no correlation between the variations in micro-albuminuria on the one hand, and the age, sex and type of diabetes on the other hand (Table III).

4. Discussion

Diabetes is a state of chronic hyperglycemia, which can lead to several types of complications, including poor diabetic nephropathy (DN) if it is not treated carefully. Micro-albuminuria is an early marker of the progression of DN [12]. Its early detection makes it possible to institute nephroprotection measures to delay this progression. The aim of our study was to assess the prevalence of diabetic nephropathy by measuring micro-albuminuria in 24-hour urine. Our study population consisted of 450 patients whose average age was 56.31 ± 12.75 years with extremes ranging from 21 to 85 years. Most of patients were aged between 40-59 (48%, $n = 216$), women (62%, $n = 279$) and type II diabetics (70%, $n = 315$). The micro-albuminuria assay found a prevalence of diabetic nephropathy at 26% ($n = 117$) in the study population. This nephropathy was predominant in type II diabetics (21.6%), women (16.9%) and in subjects over 60 years of age (15.8%).

Values found in previous studies in Senegal are higher than those in our study. The studies of Yameogo et al in 2012 and Diouf et al in 2015 found a prevalence of 36.8% and 48.7% respectively [13, 7]. In these two studies, the population consisted of type II diabetics. Actually, the prevalence of DN in type II diabetics varies depending on the country and the study. Toti et al in 2011 in Albania found a prevalence of 40.81% [13] with almost 33.3% in patients with initial diabetes. This shows the interest of screening for DN by micro-albuminuria assay. Iranian studies in 2004 and 2013 reported prevalence of 25.9% and 20.6% respectively [15, 16]. This decrease in prevalence in Iranians was also found in our study as prevalence went down from 35% in type II diabetics to 21.6% in our study. This can be explained by the size of our sample which is smaller but also by an improvement in the quality of care, in so far as subjects in our study are followed in a center which is specialized in the

treatment of diabetes. This was not the case in the study of Diouf and Yaméogo.

DN also varies by age and sex with predominance among women and the elderly. In our study, higher prevalence was reported in women and subjects aged over 60 with 16.9% and 15.8% respectively. This higher prevalence in women can be explained by the composition of our sample which was mainly composed by women (70%) but also by the fact that females are more sedentary in our society and this is a factor favoring the progression of micro-angiopathies in type II diabetics. The predominance of women in the population of diabetic was also reported by Chiheb et al who found a prevalence of DN in 68% of women [17].

Previous studies found a predominance of men in the sub-Saharan population with the studies Kadjinku in Kinshasa in 1985 and Lokrou in Côte d'Ivoire in 1994 [18, 19]. In his study, Kadjinku concluded that beyond 40 years of age, two men vs 1 woman would be at risk of having diabetes mellitus [18]. We have therefore noticed a demographic transition of the diabetic population in Sub-Saharan Africa. This transition could be explained by better awareness but also an easier access to healthcare services by women. A significant prevalence of 6% proteinuria was found in our study as was the case in the ADVANCE (Action in Diabetes and Vascular Disease) and UKPDS 64 (United Kingdom Prospective Diabetes Study) studies, which found 5% and 0.7% [20] respectively. Our results allowed us to compare the mean values of micro-albuminuria (mA) in the diabetic population with nephropathy. Higher mA was observed in subjects over 60 (80.8 ± 43.3 mg / 24h), in women (78.7 ± 47.3 mg / 24h) and in type II diabetics (67.8 ± 41.1 mg / 24h) with statistically significant differences ($p < 0.0001$) for females and the elderly. These results were reported by Diouf et al in Senegal in 2015 [7], Bouattar et al in Morocco in 2009 [12], Konta et al in Japan in 2006 [21] and Yu et al in America in 2012 [22]. However, the bivariate and multivariate analysis did not find any correlation between the variables studied and the occurrence of diabetic nephropathy. Due to the limits of this assay on 24h urine by the non-control of the collection phase, we intend to conduct a comparative study between micro-albuminuria on 24h urine and the albuminuria / creatinuria ratio (ACR) to better support our results and facilitate the monitoring of patients at risk.

5. Conclusion

Micro-albuminuria is a good marker for the prevention and diagnosis of diabetic nephropathy. Its dosage must be systematic in the care of diabetics especially in women after 50 years

Conflict of interest: the authors declare that they have no conflict of interest.

References

- [1] PUNTHAKEE, Zubin, GOLDENBERG, Ronald, et KATZ, Pamela. Définition, classification et diagnostic du diabète, du prédiabète et du syndrome métabolique. *Can J Diabetes*, 2018, vol. 42, p. S10-S15.

[2] Organisation Mondiale de la Santé (OMS). Rapport mondial sur le diabète. Genève, Suisse: Organisation mondiale de la Santé, 2016, p 88.

[3] ACH, T., HASNI, Y., MAHMOUD, N. Ben, *et al.* Prévalence de la néphropathie diabétique dans le diabète de type 1. *Néphrologie & Thérapeutique*, 2017, vol. 13, no 5, p. 369.

[4] Hamat I, Mahamat Abderrama G.Moustapha Cissé M et al. Profil de la néphropathie diabétique à l'hôpital Général de référence Nationale de N'Djamena (Tchad). *Pan Afr Med J* 2016;(24):193-201

[5] Hannedouche T.Néphropathie diabétique: signes et diagnostic. *Néphroses Learning*; Octobre 2007. www.nephrohus.org. Visité 14 Avril 2020.

[6] LOPEZ-SALL, P., CISSÉ, A., DIOP, P. A., *et al.* Facteurs de risque liés à la survenue de microangiopathies chez le diabétique sénégalais. *biochimica clinica*, 2006, vol. 30, no 1, p. 26.

[7] DIOUF, N. N., LO, G., SOW-NDOYE, A., *et al.* Evaluation of microalbuminuria and lipid profile among type 2 diabetics. *Revue medicale de Bruxelles*, 2015, vol. 36, no 1, p. 10-13.

[8] Adler AI, Stratton IM, Neil AW et al. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. *Br Med j.* 2000; 321(7258): 412- 19

[9] Barnett AH, Bain SC, Bouter P et al. Angiotensin-receptor blockade versus converting enzyme inhibition in type 2 diabetes and nephropathy. *N Engl J Med.* 2004; 351 (19): 1952-61.

[10] HALIMI, Jean-Michel, HADJADI, Samy, ABOYANS, Victor, *et al.* Microalbuminurie et excrétion urinaire d'albumine: recommandations pour la pratique clinique. *Néphrologie & thérapeutique*, 2007, vol. 3, no 6, p. 384-391.

[11] LEVEY, Andrew S., BECKER, Cassandra et INKER, Lesley A. Débit de filtration glomérulaire et albuminurie pour la détection et la stadification de l'insuffisance rénale aiguë et chronique chez l'adulte: une revue systématique. *Jama*, 2015, vol. 313, n ° 8, p. 837-846.

[12] Bouattar T, Ahid S, Benasila S et al. Les facteurs de progression de la néphropathie diabétique: prise en charge et évolution. *Néphrologie et thérapeutique* 2009; 5: 181-187.

[13] Yameogo NV, Mbaye A, Ndour M et al. Etude de la microalbuminurie et des autres facteurs de risque cardiovasculaire dans la population des diabétiques de type 2 sénégalais. *Med Afr Noire* 2012; 59: 303.

[14] Toti F, Thengilli E, Nelaj E et al. Prévalence et facteurs prédictifs de la micro-albuminurie dans un groupe des patients diabétiques albanais. *Diabetes Metab* 2011; 37: 36-108.

[15] Zakerkish M, Shahbazian HB et al. Albuminuria and Its Correlates in Type 2 Diabetic Patients. *Iran J Kidney Dis* 2013; 7: 268-76.

[16] MANAVIAT, Masoud R., AFKHAMI, Mohammad, et SHOJA, Mohammad R. Retinopathy and microalbuminuria in type II diabetic patients. *BMC ophthalmology*, 2004, vol. 4, no 1, p. 9.

[17] Chiheb S, Khadir K, Larmouni R et al. Manifestations cutanées du diabète. A propos de 358 cas. *Les nouvelles dermatologiques* 2002; 21: 64-7.

[18] Kandjiku K, Bieleli E, Bidinda M et al. Etude clinique du diabète sucré à Kinshasa. *Med Afr Noire* 1985; 32: 55-61.

[19] Lokrou A, Kouame P, Papoz L et al. Typologie du diabète sucré en côte d'Ivoire: place du diabète tropical. *Rev Fr Endocr Clin Nutr Metab* 1994; 35: 219-225.

[20] HOLMAN, Rury R., PAUL, Sanjoy K., BETHEL, M. Angelyn, *et al.* 10-year follow-up of intensive glucose control in type 2 diabetes. *New England journal of medicine*, 2008, vol. 359, no 15, p. 1577-1589.

[21] Konta T, Hao Z, Abiko H et al. Prevalence and risk factor analysis of microalbuminuria in Japanese general population; the Takahata study. *Kidney International* 2006; 70: 751-756.

[22] Yu MK, Lyles CR, Bent-Shaw SA et al. Risk factor, age and sex differences in chronic kidney disease prevalence in a diabetic cohort: The Pathways Study. *Am J Nephrol* 2012; 36: 245-51.

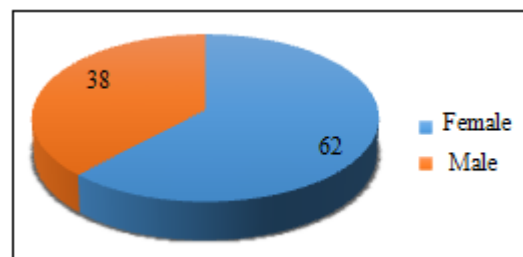


Figure 1: Distribution of the study population by sex.

Table Ia: Distribution of the population per age and type of diabetes

Age range	Type of diabetes		Total
	Type I (%)	Type II (%)	
<40 years	26 (5.8)	19 (4.2)	45 (10)
40-59 years	56 (12.4)	160 (35.6)	216 (48)
60+ years	53 (11.8)	136 (30.2)	189 (42)
Total	135 (30)	315 (70)	450

Table Ib: Distribution of the population per sex and type of diabetes

Sex	Type of diabetes		Total
	Type I (%)	Type II (%)	
Female	90 (20)	189 (42)	279 (62)
Male	45 (10)	126 (28)	171 (38)
Total	135 (30)	315 (70)	450

Table II: Determination of the prevalence of ND according to age, sex and type of diabetes

		Micro-albuminuria (mg/24h)			Total (%)
		< 30	30-300	≥ 300	
		Numbers (%)	Numbers (%)	Numbers (%)	
Age range	< 40 years	44 (9.8)	1 (0.2)	0	45 (10)
	40-59 years	162 (36)	45 (10)	9 (2)	216 (48)
	≥ 60 years	100 (22.2)	71 (15.8)	18 (4)	189 (42)
Sex	Male	121 (26.9)	41 (9.1)	9 (2)	171 (38)
	Female	185 (41.1)	76 (16.9)	18 (4)	279 (62)
Type de diabetes	Type I	106 (23.6)	20 (4.2)	9 (2)	135 (30)
	Type II	200 (44.4)	97 (21.6)	18 (4)	315 (70)

Table III: Evaluation of variations in mA based on age, sex and type of diabetes in patients with DN

		Micro-albuminuria (30-300 mg/24h)		
		Average ± ET	p	r
Age range	< 40 years	42.3±0	0.00001	-0.227
	40-59 years	45.9±30.77		
	≥ 60 years	80.8±43.3		
Sex	Male	45.6±16.3	0.00003	0.326
	Female	78.7±47.3		
Type de diabetes	Type I	63.7±48.4	0.62	0.152
	Type II	67.8±41.1		