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Risks Factors Associated with Diabetic Retinopathy at the National University Hospital Center Hubert Koutoukou Maga in Cotonou

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Abstract

Diabetic retinopathy (DR) is one of the microvascular complications of diabetes. The aim of this study was to analyze the risk factors associated with the occurrence of diabetic retinopathy (DR) at the National University Hospital Center-Hubert Koutoukou MAGA (CNHU-HKM). Patients and method: this was a descriptive and analytical cross-sectional study with prospective data collection. It was carried out over a three-month period from July 10 to October 10, 2019. It concerned all patients suffering from diabetes mellitus and who consulted in the Endocrinology department during the study period. Results: the frequency of diabetic retinopathy was 30.46% (53/174 patients). A female predominance was observed with a sex ratio (M/F) of 0.57. The main modifiable risk factors were represented by occupation and those that were not modifiable were represented by the presence of old nephropathy, glycated hemoglobin, age of discovery of diabetes and its length of service. Diabetic retinopathy is a serious condition that can ultimately lead to blindness. The frequency of DR remains high in our study.

Keywords

Associated Factors, Modifiable or Not, Diabetic Retinopathy

1. Introduction

Diabetic retinopathy (DR) is one of the microvascular complications of diabetes. It's a public health problem [1]. International Diabetes Federation (IDF) valued about a third of people with diabetes develop diabetic retinopathy [2]. In Africa, data from the literature places the overall prevalence of diabetic retinopathy at 30% (15% - 52% of people with diabetes) [3]. It is a major cause of loss vision and is the leading cause of blindness before the age of 55 [4]. The cost of DR before the stage of blindness is relatively low compared to that of other complications of diabetes. However, the cost of blindness is much higher, and is among the most costly complications of diabetes [5]. Many studies found that diabetic retinopathy was associated to several risk factors [6] [7]. It therefore appears important to know the factors linked to the occurrence of diabetic retinopathy in order to better control them in order to reduce the prevalence of this condition.

2. Patients and Method

This was a cross-sectional descriptive and analytical study with prospective data collection. It was carried out over a three-month period from July 10 to October 10, 2019. It was represented by a group of patients suffering from diabetes mellitus and who consulted in the Endocrinology department during the study period. Were included in the study, patients aged at least 18 years, suffering from diabetes mellitus (type 1 or 2), having consulted in the Endocrinology department of the CNHU-HKM, undergoing a background examination eye in the Ophthalmology department and consenting to the study. All patients with blindness and pregnant women were excluded from the study. An exhaustive recruitment of all patients meeting our study criteria was carried out. The dependent variable was represented by diabetic retinopathy. The independent variables were for non modifiable risk factors which were age, sex, type of diabetes, duration of diabetes, age of onset of diabetes, family history of diabetes and high blood pressure. Modifiable risk factors such as level of education, occupation, overweight, obesity and abdominal obesity, alcoholism, smoking, physical inactivity, nephropathy, neuropathy, treatment with insulin, oral antidiabetics (ADO) and herbal teas, diabetes imbalance (glycated hemoglobin > 7%), LDL and total hypercholesterolemia, hypertriglyceridemia and the presence of a significant 24-hour microalbuminuria.

Data collection was carried out by a questionnaire and a smartphone on which the Kobo-collect software for data recording was installed. All patients received a free fundus in the ophthalmology department. Data analysis was performed with SPSS software version 25.0. Proportions were calculated for qualitative variables. Means and standard deviations were calculated for the description of quantitative variables. Bivariate analysis was performed to identify associated factors. The comparison of the proportions was made using Fisher's tests, Yates's Chi^2 and Pearson's Chi^2. The Fisher test was considered when the smallest theoretical size was less than or equal to 3, Yates' Chi^2 when it is greater than 3 and less than

or equal to 5 and Pearson's Chi^2 when it is strictly greater than 5. The difference was statistically significant for a p-value less than 0.05. The strength of the association was assessed using the Odds Ratio (OR) and its 95% confidence interval (95% CI OR). The tables and figures were performed using Microsoft Office Word and Excel version 2016 software. The patients' oral, free and informed consent was obtained. All data collected anonymously during the investigation was used only for this study and was kept strictly confidential. The difficulty encountered was the non-availability of patients to honor ophthalmology appointments.

3. Results

3.1. Frequency of Diabetic Retinopathy

A total of 174 subjects were included, of which 53 had diabetic retinopathy, then a frequency of 30.46%.

3.2. Risks Factors Associated with Diabetic Retinopathy

3.2.1. Modifiable Risk Factors

Sociodemographic Characteristics

Table 1 shows the distribution of diabetic retinopathy according to marital status, level of education, professional status and religion.

Occupation was the only modifiable socio-demographic factor associated with the occurrence of diabetic retinopathy (p = 0.035). Retired people (odds ratio at 13.51 with a confidence interval between 1.70 and 107.25) as well as employees

Table 1. Diabetic retinopathy (DR) according to marital status, level of education, professional status and religion.

	Total	DR		OR	IC 95%	p-value
		Yes	%			
Marital status						
Married	137	44	32.12	1.47	[0.64 - 3.38]	p = 0.360
Unmarried	37	09	24.32	1		
Educational level						
Not in school/Primary	42	15	35.71	1.37	[0.65 - 2.86]	p = 0.238
Secondary/ university	132	38	28.79	1		
Professional situation						
Retired	62	25	40.32	2.02	[1.04 - 3.93]	p = 0.035*
Working	112	28	25.00	1		
Religion						
Christian	149	45	30.20	0.91	[0.37 - 2.28]	p = 0.856
others	25	08	32.00	1		

* = significative p.

(odds ratio at 11.51 with a confidence interval between 1.42 and 92.74) were the most affected by diabetic retinopathy.

3.2.2. Behavioral Factors

Table 2 illustrates the distribution of the occurrence of diabetic retinopathy (DR) according to behavioral factors.

There was no statistically significant association between behavioral factors and the occurrence of DR.

3.3. History of Peripheral Neuropathy and Nephropathy

Table 3 shows the distribution of the frequency of diabetic retinopathy (DR) according to the history of peripheral neuropathy and nephropathy.

Table 2. Occurrence of diabetic retinopathy according to behavioral factors.

	Total	RD		OR	IC 95% OR	p-value
		yes	%			
Harmful alcohol consumption (alcohol consumption over 20 g/day for women and 30 g/day for men)						
Yes	01	00	-	-	-	-
No	173	53	30.64	-	-	
Risky alcohol consumption (alcohol consumption over 60 g/day)						
Yes	16	04	25.00	0.74	[0.22 - 2.41]	p = 0.831
No	158	49	31.01	1		
Smoking						
yes	01	00	-	-	-	-
No	173	53	30.64	-	-	
Physical activity						
Insufficient	157	49	31.21	1.47	[0.45 - 4.75]	p = 0.513
Sufficient	17	04	23.53	-		

Table 3. Frequency of DR according to the history of peripheral neuropathy and nephropathy.

	Total	DR			IC 95% OR	p-value
		Yes	%			
Peripheral neuropathy						
Yes	74	26	35.14	1.46	[0.76 - 2.80]	p = 0.249
No	100	27	27.00	1		
Nephropathy (N = 61)						
Yes	34	14	41.18	4.02	[1.13 - 14.22]	p = 0.024
No	27	04	14.81	1		

There was a statistically significant association between DR and the existence of nephropathy (p = 0.024). Patients with nephropathy were more likely to have DR than others (odds ratio 4.02 with a confidence interval of [1.13 - 14.22]).

3.4. Antidiabetic Treatment

Table 4 shows the distribution of the occurrence of DR according to the antidiabetic treatment.

There was no statistically significant association between diabetes treatment and DR.

3.5. Anthropometric Factors

Table 5 summarizes the distribution of the occurrence of DR according to anthropometric factors.

There was no statistically significant association between these factors and the existence of diabetic retinopathy.

Table 4. Distribution of DR according to antidiabetic treatment.

	Total	DR		OR	IC 95% OR	p-value
		Yes	%			
HDM	09	02	22.22	0.67	[0.13 - 3.40]	
HDM + Insuline	22	10	45.45	1.97	[0.79 - 4.95]	p = 0.249
MHD + OAD + Insuline	06	01	16.67	0.47	[0.05 - 4.19]	
Tisane	02	00	-	-	-	
HDM + OAD	135	40	29.63	1		

HDM = Hygiene and dietetic measures; OAD = Oral antidiabetics.

Table 5. Distribution of DR according to anthropometric factors.

	Total	RD		OR	IC 95% OR	p-value
		Yes	%			
Abdominal obesity according to NCEP*						
Yes	104	28	26.92	0.66	[0.34 - 1.27]	p = 0.216
No	70	25	35.71	1		
Abdominal obesity according to IDF**						
Yes	143	44	30.77	1.08	[0.46 - 2.54]	p = 0.848
No	31	09	29.03	1		
Body Mass Index (BMI)						
overweight/Obesity	123	37	30.08	0.94	[0.46 - 1.90]	p = 0.866
Thinness/Normal	51	16	31.37	1		

NCEP* = National Cholesterol Prevention Program; IDF** = International diabetes federation.

3.6. Biological Parameters

Table 6 shows the distribution of the occurrence of DR according to the biological parameters.

Glycemic imbalance was strongly associated with the development of DR ($p < 0.001$). People who had glycated hemoglobin ≥ 7% were the most affected by this condition (odds ratio at 3.36 with a confidence interval of [1.60 - 7.04]). There was an association between 24-hour microalbuminuria and the existence of DR. Subjects with significant 24-hour microalbuminuria (>30 mg) were more likely to have DR ($p = 0.066$).

3.7. Non-Modifiable Risk Factors

Sociodemographic characteristics

Table 7 shows the distribution of the frequency of DR by age, sex and ethnicity.

There was no statistically significant association between age, gender, ethnicity and DR.

3.8. History of High Blood Pressure and Familial Diabetes

Table 8 shows the distribution of the frequency of DR according to the history of high blood pressure and familial diabetes

There was a significant association between diabetic retinopathy and high blood pressure ($p = 0.002$). DR was much more common in people with hypertension (odds ratio of 3.45 with a confidence interval of [1.49 - 7.96]).

Table 6. Distribution of DR according to the biological parameters.

	Total	RD		OR	IC 95% OR	p-value
		Yes	%			
Total cholesterol (N = 97)						
>2.25 g/l	13	00	-	-	-	-
≤2.25 g/l	84	27	32.14	-	-	
LDL cholesterol (N = 89)						
>1.5 g/l	14	01	07.14	0.16	[0.02 - 1.32]	p = 0.115
≤1.5 g/l	75	24	32.00	1		
Triglyceridemia (N = 96)						
>1.5 g/l	08	01	12.50	0.36	[0.04 - 3.07]	p = 0.442
≤1.5 g/l	88	25	28.41	1		
Glycated hemoglobin (N = 159)						
>7%	83	34	40.96	3.36		p < 0.001*
≤7%	76	13	17.11	1		
24-hour micro albuminuria (N = 61)						
>30 mg	33	13	39.39	2.99	[0.90 - 9.85]	p = 0.066
≤30 mg	28	05	17.86	1		

* = significative p.

Table 7. Frequency of DR by age, sex and ethnicity.

	Total	DR		OR	IC 95% OR	p-value
		yes	%			
Age (years)						
>57	87	28	32.18	1.17	[0.61 - 2.24]	p = 0.621
≤57	87	25	28.74	1		
Sex						
Male	75	23	30.67	1.01	[0.53 - 1.95]	p = 0.958
Female	99	30	30.30	1		
Ethnicity						
local language	110	32	29.09	0.84	[0.43 - 1.63]	p = 0.607
Others	64	21	32.81	1		

Table 8. Frequency of DR according to the history of high blood pressure (HBP) and familial diabetes.

	Total	DR		OR	IC 95% OR	p-value
		Yes	%			
HBP						
Yes	120	45	37.50	3.45	[1.49 - 7.96]	p = 0.002*
N	54	8	14.81	1		
Duration of HBP (years) (N = 120)						
>7	58	19	32.76	0.67	[0.32 - 1.42]	p = 0.299
≤7	62	26	41.94	1		
Familial diabetes						
Yes	119	37	31.09	1.10	[0.54 - 2.21]	p = 0.789
No	55	16	29.09	1		
Familial diabetes relationship (N = 119)						
first-degree relative	98	28	28.57	0.53	[0.20 - 1.40]	p = 0.199
second degree relative	21	09	42.86	1		

* = significative p.

3.9. Characteristics of Diabetes

Table 9 shows the distribution of the occurrence of DR according to the age of discovery of diabetes, the type of diabetes and its duration.

Duration of diabetes was significantly associated with the occurrence of DR ($p < 0.001$). Subjects diagnosed with diabetes for more than 5 years were more affected by DR than others (odds ratio 5.02 with a confidence interval of [2.39 - 10.50]). There was also a statistically significant association between age of discovery of diabetes and DR ($p = 0.029$). Patients whose age was 48 years or less at the time of diagnosis of diabetes were the most affected by this condition (odds ratio 2.07 with a confidence interval of [1.06 - 4.04]).

Table 9. Distribution of DR according to age of onset of diabetes, type of diabetes and its duration.

	Total	DR		OR	IC 95% OR	p-value
		Yes	%			
Duration of diabetes (years)						
>5	90	41	45.56	5.02	[2.39 - 10.50]	p < 0.001*
≤5	84	12	14.29	1		
Age onset of diabetes (en années)						
≤48	90	34	37.78	2.07	[1.06 - 4.04]	p = 0.029*
>48	84	19	22.62	1		
Type of diabetes						
Type 2	167	52	31.14	2.71	[0.31 - 23.11]	p = 0.676
Type 1	07	01	14.29	1		

*=significative p.

4. Discussion

4.1. Frequency of Diabetic Retinopathy

The frequency of DR was 30.46% in our study. It is close to the 33% of Nwosu *et al.* [6] in Nigeria in 2000 and 36.6% of Tchabi *et al.* [7] in Benin in 2012. However, Abouki *et al.* [8] in Benin in 2016, Kouassi *et al.* [9] in Côte-d'Ivoire in 2018 and Diallo *et al.* [10] in Burkina-Faso in 2014 found higher frequencies of 43.33%, 45% and 47.1% respectively. Rajoana *et al.* [11] in 2016 in Madagascar reported a higher frequency of 65.8%. These results illustrate the importance of DR within our populations and call for our actions to be focused on preventive measures. In contrast, Magulike *et al.* [12] in 2003 in Nigeria, Omolase *et al.* [13] in 2010 in Nigeria, Assavedo *et al.* [14] in 2016 in Benin, Djagadou *et al.* [15] in 2017 in Togo and Maammar *et al.* [16] in 2013 in Algeria found lower frequencies respectively 12.75%, 15%, 17.46%, 22.73% and 25.37%. The disparity in these frequencies may be related to the difference in size and to the sampling techniques that differ from one study to another.

4.2. Risk Factors for Diabetic Retinopathy

Modifiable Risk Factors

Level of Education

In our study, the frequency of DR was slightly higher in people with a low level of education (out of school/primary) than in others (35.71% versus 28.79%). This result agrees with that of Abouki *et al.* [8] in Porto-Novo in Benin in 2016 who reported that this condition was predominant among illiterates (55.36%) and subjects with a primary education level (45.45%). In contrast, Cui *et al.* [17] in China in 2019 noted that DR was predominantly present in people with a high level of education (secondary/higher), *i.e.* 51.9%. In all cases, the level of education is not a risk factor for DR (odds ratio at 1.37 with a 95% confidence interval

between 0.65 and 2.86; p = 0.395).

4.3. Professional Situation

Some authors have found a higher proportion of DR among the unemployed. This is the case with Abouki *et al.* [8] in Porto-Novo in Benin (57.14%) in 2016 and from Ben *et al.* [18] in Tunisia (40%) in 2016. This result could be explained by the social situation of unemployed people who are unable to provide for correct and efficient management of their condition. It emerges from this study that occupation constitutes a risk factor for DR (for retirees, odds ratio at 2.02 with a 95% confidence interval between 1.04 and 3.93; p = 0.035).

4.4. Antidiabetic Treatment

The frequency of DR was higher in subjects taking insulin (45.45%). The same observation was made by Pirie *et al.* [19] in 2014 in South Africa. In 2012 in Rwanda, Giraneza *et al.* [20] meanwhile, reported a lower proportion than ours, 37.17%. These differences could be explained by the sample sizes of these studies. Treatment regimen is not a risk factor for DR (odds ratio at 1.97 with a 95% confidence interval between 0.79 and 4.95; p = 0.395).

4.5. Diabetic Nephropathy

Diabetic retinopathy was more represented in people with diabetic nephropathy at 41.18% (vs. 14.81%). This result is similar to that of Assavedo *et al.* [14] in Parakou in Benin in 2014 who reported that 21.9% (compared to 5.8%) of subjects with diabetic nephropathy developed parallel DR, but also that of He *et al.* [21] in China (43.06% against 25.33%) in 2012. However, Rasoulinejad *et al.* [22] in Iran in 2015 objected that DR was present in almost equal proportion in patients already with the stage of diabetic nephropathy (67.74%) and in those who are not (64.53%). However, diabetic nephropathy is a risk factor for DR (odds ratio 4.02 with a 95% confidence interval between 1.13 and 14.22; p = 0.024).

4.6. Glycemic Imbalance

DR was present in 40.96% of patients with poor glycemic control. This same observation was made by Djrolo *et al.* [23] in Benin (94.6%) in 2014, Lopez *et al.* [24] in Spain (16.82%) in 2017. A UKPDS study in type 2 diabetics demonstrated the role of glycemic imbalance in the incidence and progression of DR [25]. Diabetes imbalance is indeed a risk factor for DR (odds ratio at 3.36 with a 95% confidence interval between 1.60 and 7.04; p < 0.001).

4.7. Microalbuminuria

In our study, DR was predominantly present at 39.39% in diabetics who had significant microalbuminuria (>30 mg/24h). This result is comparable to those of Abouki *et al.* [8] in Porto-Novo in Benin (66.67%) in 2016 and Berkia *et al.* [25] in Morocco (53.1%) in 2014 but in higher proportions. However, microalbumi-

nuria is not a risk factor for DR (odds ratio at 2.99 with a 95% confidence interval between 0.90 and 9.85; p = 0.066).

4.8. Type of Diabetes

DR was more common in type 2 diabetes in our study at 31.14% versus 14.29%. In fact, it usually occurs after 7 years of diabetes in type 1 diabetics, and 20% of type 2 diabetics had it when their diabetes was discovered [26]. However, in 2015 in Rabat, Morocco, Andaloussi *et al.* [27] obtained similar results for the two types of diabetes (40.5% for type 1 and 38.9% for type 2) with regard to the occurrence of this condition. However, the type of diabetes is not a risk factor for DR (odds ratio 2.71 with a 95% confidence interval between 0.31 and 23.11; p = 0.676).

4.9. Duration of Diabetes

Many studies have shown an increase in the frequency of DR with the age of diabetes. Mallika *et al.* [28] noted in Malaysia in 2011 a faster development of DR when the age of diabetes is greater than 15 years. Cui *et al.* [17] in China in 2019 found as proportions of DR 15.02%, 43.59% and 66.67% respectively in subjects diagnosed for less than 5 years, 5 to 10 years and more than 10 years. The duration of diabetes is therefore a risk factor for DR (odds ratio 5.02 with a 95% confidence interval between 2.39 and 10.50; p < 0.001).

4.10. Age Onset of Diabetes

People diagnosed with diabetes at younger ages (≤48 years) had more DR (37.78%). This result was similar on that obtained in 2016 by Zou *et al.* [15] in China who found that young age at discovery of diabetes (<45 years) is a factor favoring the development of DR. In contrast, Ahmed *et al.* [29] in 2016, Saudi Arabia found that DR was more common when the age of discovery of diabetes was over 45 years (70.6% vs. 58%). This difference could be explained by the fact that this study only took into account type 2 diabetics. Thus, the age onset of diabetes is a risk factor for DR (odds ratio at 2.07 with a 95% confidence interval between 1.06 and 4.04; p = 0.029).

4.11. High Blood Pressure

Based on the literature, there is a strong link between DR and high blood pressure. According to a study by the UKPDS (United Kingdom Prospective Diabetes Study), strict balancing of blood pressure in type 2 diabetics was highly beneficial because it would reduce the incidence of microvascular complications by 37% and reduce the increase in DR by 34% [9]. In Senegal in 2008, De Médeiros-Quenum *et al.* [30] noted that 77.77% of hypertensive patients presented with DR. Conversely, in Porto-Novo in Benin in 2016, Abouki *et al.* [8] objected that 50% of non-hypertensive diabetics developed DR while 40.91% of hypertensive patients were affected. In our study, DR was more found in hyper-

tensive than in non-hypertensive (37.50% versus 14.81%). High blood pressure is also a risk factor for DR (odds ratio at 3.45 with a 95% confidence interval between 1.49 and 7.96; p = 0.002).

5. Conclusion

Diabetic retinopathy is a serious condition that can ultimately lead to blindness. The frequency of DR remains high and requires consideration of risk factors in the monitoring of diabetics in order to prevent this preventable cause of blindness. The prevention and promotion of ocular eye health requires large-scale awareness of these risk factors identified in our context.

Conflicts of Interest

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

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