Research Article

Periodontitis Increases Risk of Peripheral Arterial Occlusive Disease in Diabetics Subjects Living in Cameroon

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Abstract

The aim of our study was to evaluate the relationship between Peripheral Arterial Occlusive Disease (PAOD) and Periodontitis in Diabetics subjects followed in Douala General Hospital, Cameroon.

Materials and Method: We conducted a cross-sectional study from January 1 to March 20, 2020. To be included in the study, subjects had to be either type 1 or type 2 diabetics, at least 18 years of age and

benefiting from either inpatient or outpatient followed up in the internal medicine department. Ankle Brachial Index (ABI) were measured for each participant with manual sphygmomanometer and pocket Doppler. Periodontitis was classified based on pocket depth (PD) and clinical attachment (CAL) values according the Centers For Disease Control and Prevention and the American Academy of Periodontology 2007 (CDC/AAP) All statistical analyses were performed using Epi Info7 software. Logistic regression analysis was performed to determine factors associated to PAOD in our sample.

Results: A total of 100 patients were recruited. Mean periodontal parameters such as PD, CAL, number of sites with PD>4mm, number of sites with CAL>3mm were significantly higher in PAOD diabetics subjects compared to those without PAOD. After multivariate logistic regression, the factors remaining associated to PAOD were periodontitis (OR=3,60 [1,12-11,53]) and hypercholesteremia (OR=5,99 [2,04-17,55]).

Conclusion: Management of periodontitis may reduce the risk of having PAOD in diabetic subjects followed at the Douala General Hospital, Cameroon.

Keywords: Periodontitis; Peripheral Arterial Occlusive Disease; Ankle Brachial Index; Diabetes; Cameroon

1. Introduction

Peripheral arterial occlusive disease (PAOD) reflects damage to the arterial network of the lower limbs by the process of atherosclerosis. It affects more than 200 million people worldwide [1]. Diabetes is a potent risk factor for PAOD with major amputation of the lower limbs as main complication [1, 2]. The frequency of PAOD is 22% in black African diabetics [2]. PAOD diagnosed by finding an Ankle Brachial Index (ABI) value less than 0.90 [3]. Periodontitis is an inflammatory disease linked to an imbalance of the oral flora leading to an irreversible destruction of the periodontal attachment system. The prevalence of periodontitis varies from 20 to 50% in the general population [4]. In Cameroon, its frequency is 15% [5]. Etiopathogenic mechanisms of periodontitis are complex and result from the imbalance between bacterial aggression and the host's defenses on one hand, and general, systemic and environmental risk factors on the other [6].

The diagnosis of periodontitis is made on the basis of certain clinical signs such as clinical attachment loss (CAL), presence of periodontal pocket, gingival bleeding and radiological signs corresponding to bone resorption. The role of diabetes in the pathogenesis of periodontal disease has been highlighted by several studies [7, 8]. Nascimento and al. have shown that diabetes increased the risk of periodontitis in adults (RR =1.86 [1.3-2.8]) [8]; On the other hand, current data suggest that periodontal disease is associated to cardiovascular diseases linked to atherosclerosis such as coronary artery disease, cerebrovascular disease and peripheral arterial disease [9,10]. The link between periodontitis and peripheral artery disease has been the subject of some publications [9-14]. Recent data suggest that patients with PAOD have 1.70 times more risk of developing periodontitis compared to those without PAOD [10]. In addition, the beneficial effect of periodontal therapy on endothelial function has also been described [10, 15]. Because of the high cardiovascular and periodontal risks of the diabetic subject, it seemed relevant to us to assess the link between periodontitis and PAOD in diabetic subjects

followed up at the Douala General Hospital.

2. Materials and Method

We conducted a cross-sectional study in the internal medicine department of the Douala General Hospital from January 1 to March 20, 2020. To be included in the study, subjects had to be either type 1 or type 2 diabetics, at least 18 years of age and benefiting from either inpatient or outpatient followed up in the internal medicine department. Diabetic patients who did not have a biological assessment (LDL cholesterol level) dating less than 1 month as well as those who presented any event affecting assessment of ABI, namely; pregnancy, history of vascular surgery, local diseases compromising assessment of ABI, patients with short-term life-threatening alterations in vital function were not included. Likewise, all diabetic patients who presented any event compromising assessment of periodontitis, namely any patient who received periodontal treatment during the last 6 months, and/or under antibiotic therapy, and those with less than 50% of teeth per sextant were excluded from the study.

2.1 Data collected and variables definitions

For each participant, a pre-tested questionnaire was used to collect information related to marital status, age, gender, smoking, medical history of diabetes, hypertension, obesity, LDL cholesterol level and medications. This was done through patients' medical files. The fasting capillary blood glucose test was carried out using glucometers. The weight, height, body mass index (BMI), and ABI were measured by a trained practicing nurse. Periodontal examination was conducted by periodontist.

2.2 ABI assessment

Brachial and ankle pressures were measured for each participant after an adequate rest of at least 5 minutes in a supine position. A manual sphygmomanometer and pocket Doppler device with a probe to listen to the flow of the brachial, dorsal pedal, and posterior tibial arteries were used. Brachial pressures were measured bilaterally, and were repeated if the difference was > 10 mm Hg between the two arms. Ankle pressures were determined with cuffs placed proximal to the malleoli. The ABI was calculated by dividing the highest systolic ankle pressure (either posterior tibial or dorsal pedal) in each leg by the highest systolic brachial pressure.

2.3 Periodontal examination

A partial mouth periodontal examination was performed on ten index teeth, namely, 17, 16, 11, 26, 27, 37, 36, 31, 46, 47. Periodontal probing was carried out using a WHO periodontal probe at 4 sites per tooth, mesio and disto vestibular, mesio and disto lingual, or mesio and disto-palatine. Periodontal parameters assessed were oral hygiene, pocket depth (PD) and CAL. The values obtained after probing were entered on the survey sheet. The PD measured corresponded to the distance from the gingival margin to the bottom of the sulcus. CAL corresponded to the distance from the cementum enamel junction to the bottom of the sulcus. If an index tooth was absent it was replaced by another tooth belonging to the same sextant. Teeth with significant coronary decay as well as cervical fillings that did not allow the cementum enamel junction to be assessed were not considered. Oral hygiene was evaluated using plaque index scores according to Silness and Löe, 1964.

Score 0: no plaque;

Score 1: thin film of plaque in contact with the marginal gingiva visible only after exploration with the probe;

Score 2: moderate accumulation of plaque in contact with the marginal gingiva; no plaque in the inter-dental spaces; deposits visible to the naked eye;

Score 3: large accumulation of plaque in contact with the marginal gingiva; presence of plaque in the inter-dental spaces.

In the event of a tooth loss or significant or total coronary destruction, no score was assigned. The final score was the total score divided by the number of sites examined. Periodontitis were classified based on PD and CAL values according the Centers For Disease Control and Prevention and the American Academy of Periodontology 2007 (CDC/AAP) as Mild periodontitis (at least 2 inter proximal sites with CAL ≥ 3mm on different teeth and at least 2 inter proximal sites with PD ≥ 4mm or at least 1 inter proximal site with PD ≥ 5mm); moderate periodontitis (at least 2 inter proximal sites with CAL ≥ 4mm on different teeth or at least 2 inter proximal sites with PD ≥ 5mm on different teeth); Severe periodontitis (at least 2 inter proximal sites with CAL ≥ 6mm on different teeth or at least 2 inter proximal sites with PD ≥ 5mm on different teeth). The variables measured were defined as follows:

- PAOD: ABI < 0.9;
- Hypertension: subjects with diagnostic of hypertension in their medical file and under anti-hypertensive treatment followed in the internal medicine department of Douala General Hospital;
- Diabetes: subjects with diagnostic of diabetes in their medical file and under anti-diabetic treatment followed in the internal medicine department of Douala General Hospital;
- Smoking: was considered as smoker, anyone declaring to smoke at least 1 cigarette per day;
- Alcoholism: was considered as an alcohol consumer, anyone declaring to drink at least one alcoholic drink per day;
- Obesity: BMI ≥ 30 Kg/m²;
- Hypercholesterolemia: was defined on the basis of lipid-lowering treatments and/or LDL-cholesterol level > 1.5g/l.

2.4 Statistical analysis

All statistical analyses were performed using Epi Info7 software. The Students' t test was used to compare the means of quantitative variables; the X^2 test was used to compare qualitative variables. Logistic regression analysis was performed to determine factors associated to PAOD in our sample. The significance level for all analyses was set at $p < 0.05$.

2.5 Ethical considerations

The study was conducted in accordance with the Helsinki Declaration and approved by the Faculty of Medicine and Pharmaceutical Sciences of the University of Douala, and registered at the Ethics Committee of the faculty under the number 2164 CEI-Udo/01/2020/T.

3. Results

3.1 General characteristics of the sample

A total of 100 diabetics patients were included in the study, 95% of them were type 2 diabetics. Over 55% were women and the male/female sex ratio was 0.82. A total of 27 patients were diagnosed with PAOD. Regarding our population with PAOD, 17 patients were women (62.97%) and 10 were men (37.03%). Overall, 52 subjects in our sample suffered from PD. Mean periodontal parameter were significantly higher in PAOD diabetics subjects compared to those without PAOD. The general characteristics of the sample are represented in tables 1 and 2, and in figure 1.

3.2 Factors associated with PAOD

After multivariate logistic regression, the factors remaining associated to PAOD were periodontitis (OR=3,60 [1,12-11,53]) and hypocholesteremia

(OR=5,99 [2,04-17,55]). The results of analysis of the relationship between PAOD and other subjects' characteristics are shown at Tables 3 and 4.

Variables	Mean	Standard deviation	Minimum	Maximum	Median
Age (years)	60.04	10.27	30.00	84.00	60.10
ABI	1.04	0.17	0.53	1.42	1,10
Glycaemia (g/l)	1,68	0.84	0,70	4.75	1.36
LDL-cholesterol (g/l)	1.09	0.25	0.40	1.75	1.2
Diabetes duration (years)	7.81	6.49	1.00	30.00	8.00

ABI: ankle brachial index; LDL: low density lipoprotein

Table 1: General parameters of the study.

Periodontal Parameters (Mean)	PAOD		p
	Yes (n= 27)	No (n=73)	
	Mean ± Sd	Mean ± Sd	
PI	0.44 ± 0.80	0.48 ± 0.83	>0.5
PD	3.48 ± 0.71	2.54 ± 1.09	<0.00001
CAL	0.84 ± 0.57	0.53 ± 0.69	0.042
Number of sites with PD ≥ 4mm	13.44 ± 6.48	6.52 ± 8.99	<0.00001
Number of sites with PAC ≥ 3mm	6.81 ± 4.00	3.07 ± 4.50	<0.00001

PAOD: Peripheral Arterial Occlusive Disease; Sd: standard deviation; PI: plaque index; PD: pocket depth; CAL: clinical attachment loss.

Table 2: Periodontal parameters of subjects.

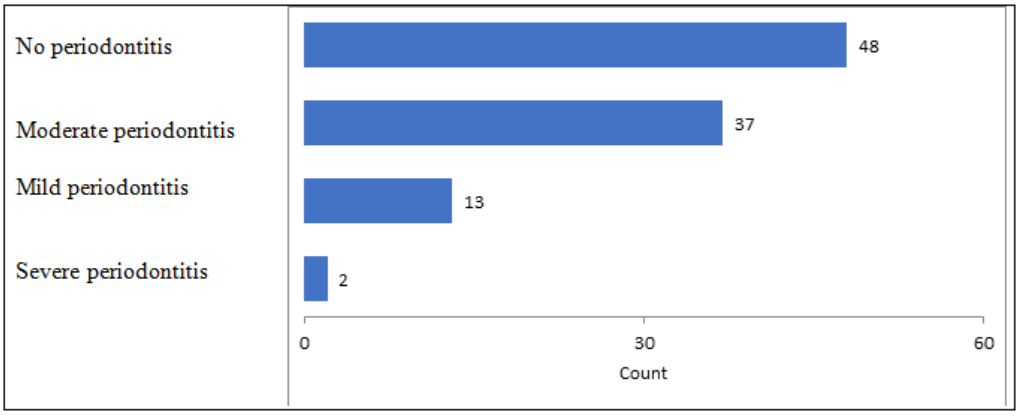

Figure 1: Frequency of periodontitis in the sample.

Variables		PAOD				OR (CI95%)	p
		Yes		No			
		n	%	n	%		
Hypertension	No	7	25.9	28	38.4	1.77 (0.66-4.74)	0.251
	Yes	20	74.1	45	61.6		
Hypercholesterolemia	No	11	40.7	63	86.3	9.16 (3.31-25.33)	0.001
	Yes	16	59.3	10	13.7		
Obesity	No	7	25.9	25	34.2	1.48 (0.55-3.99)	0.43
	Yes	20	74.1	48	65.8		
Smoking	No	25	92.6	66	90.4	0.75 (0.14-3.87)	0.736
	Yes	2	7.4	7	9.6		
Periodontitis	No	5	18.5	43	58.9	6.30 (2.14-18.51)	0.001
	Yes	22	81.5	30	41.1		

PAOD: Peripheral Arterial Occlusive Disease; OR: odd ratio; CI95%: 95% confidence interval.

Table 3: Factors associate to PAOD, univariate analysis.

Risk Factor	OR (CI95%)	p-value
Hypercholesterolemia	5.99 (2.04-17.55)	0.001
Periodontitis	3.60 (1.12-11.53)	0.031

OR: odd ratio, CI95%: 95% confidence interval

Table 4: Significant risk factors associate to PAOD, multivariate analysis.

4. Discussion

In this cross-sectional study, we found that diabetic subjects suffering from periodontitis were 3 times at risk of developing PAOD after adjusting for hypercholesterolemia. This study also provides the evidence that mean periodontal parameters of PAOD diabetics such as PD, CAL, sites with PD ≥ 4mm and sites with CAL ≥ 3mm were significantly higher compared to those without PAOD. These results are similar to those reported in the literature regarding the association between periodontitis and PAOD [11-15]. In fact, the systematic review by Kaschwish et al identified 9 studies out of 31 which found a positive association between periodontitis and PAOD [12]. The first published report was made by Mendez et al in a study conducted in 1998 [13]. It reported that the risk of developing PAOD was 2.27 [1.32-3.9] times higher in men with periodontitis at baseline, compared to those without periodontitis or those with mild periodontitis.

Similarly, Lu et al in 2008, showed that periodontitis was significantly associated with PAOD in 172 subjects (OR = 2.3 [1.2–4.2]) [14]. Chen et al in 2008, in Japan observed in a case-control study that periodontitis was significantly associated with PAOD after adjusting for age, gender, diabetes and tobacco (OR = 5.5 [1.6–18.9])

[15]. Calapkorur et al in 2017, found that periodontitis increased the risk of having PAOD by 5.8 [1.5-21.9] after adjusting for age, diabetes, hypertension and BMI. However, in this study the authors did not find a significant association between clinical periodontal parameters and peripheral arterial disease in 60 participants [16].

Yang et al in 2018, via a meta-analysis on 4,307 participants showed a significantly increased risk of PD in the group of patients with PAOD compared to patients who were free from PAOD (RR = 1.70 [1.25-2.29]) [11]. The pathophysiological mechanisms between PAOD and periodontitis are complex and four of them have been resumed in the systematic review of Kaschwich in 2019, to explain this association [12, 18-22]: (1) oral bacteremia is thought to be responsible for the penetration of microorganisms into the bloodstream. origin of damage to the arterial wall [18, 19]; (2) periodontal inflammation is thought to be responsible for the release of pro-inflammatory mediators at the systemic level causing an acute phase reaction, which is pro-atherogenic [20, 21]; (3) the specific components of the pathogens would trigger an immune response from the host, thus promoting autoimmunity [22]; and finally, (4) the specific bacterial toxins produced by oral pathogenic bacteria would have pro-atherogenic effects. Recent works support the fact that periodontal disease and occlusive peripheral artery disease share at least one important predisposing genetic risk haplotype located on chromosome 9p21.3 in a locus called ANRIL/CDKN2B-AS1 [22].

In our study, the global frequency of periodontitis in diabetics patients was 52% and 81% for PAOD diabetics. This figure is higher than that described in previous works on diabetic populations in Cameroon, which had under 12% [23]. This could be explained by the fact that our current sample consisted of 100 diabetic patients versus 40 subjects in the previous study. Likewise, the frequency of severe periodontitis in our global population was low (0.38%), and 71% subjects had moderate periodontitis. Our results differ from those reported by Khumaedi et al in 2018, who found respectively 16.5% of moderate periodontitis, and 75.3% of severe forms in 97 diabetic patients in Indonesia [24]. According to the Global Burden of Disease study published in 2010, severe periodontitis was the sixth most common medical condition among the 291 diseases [25]. Its prevalence is estimated at 11.2% and severe periodontitis has been associated with the occurrence of ischemic cardiovascular events [9, 25].

In this work, hypercholesterolemia increased by 6 times the risk of developing PAOD. Our results corroborate with those in recent literature. In fact, age, smoking, diabetes, obesity, hypercholesterolemia and hypertension are known risk factors for PAOD reported in the literature [1]. Partial mouth periodontal examination could constitute one of the limitations of this study due to the small number of sites examined. Indeed, the periodontal examination in the full mouth constitutes the reference for determining the periodontal state of an individual. Although a thorough examination is possible in the clinical setting, it requires more time and resources during an epidemiological investigation [26]. The 10 index teeth specified in partial registration were identified as the best, in the worst periodontal condition estimate of the mouth. Likewise, the lack of doppler ultrasound use in our study would have contributed to the underestimation of the ABI measurement in the presence of mediacalcosis [1, 3].

5. Conclusion

Periodontitis increased 3 times more risk of developing PAOD in diabetics subjects living in Cameroon after adjusting for hypercholesterolemia . Management of periodontitis may reduce the risk of having PAOD in diabetic subjects followed at the Douala General Hospital, Cameroon.

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