PanAfrican Medical Journal

Open Access

Research

# Micro and macrovascular complications of diabetes mellitus in Cameroon: risk factors and effect of diabetic check-up - a monocentric observational study

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Key words: Diabetes mellitus, Microangiopathy, Macroangiopathy, HbA1c, Diabetic check-up, Cameroon

Received: 03/10/2012 - Accepted: 20/04/2013 - Published: 18/08/2013

**Abstract**

**Introduction:** The objective of this study was to evaluate the prevalence of vascular complications among diabetes patients (DP), to find out the relationship with risk factors and to assess the effect of diabetic check-up (DC) in the onset of these complications. **Methods:** Clinical and laboratory data of DP followed between 2000 and 2009 were retrospectively analyzed. Those with at least one DC were selected (140 out of 538). Risk factors were checked and listed. Prospectively, an electrocardiogram (ECG) was recorded for 121 of them. **Results:** The sample was constituted of 78 (56%) men and 62 (44%) females; mean age was 55 ± 12 years. Type 2 Diabetes accounted for 94.3%. Microangiopathy distribution was: retinopathy = 23.6%, nephropathy = 25% and neuropathy = 40%. Within macroangiopathy prevalence was: 5% for stroke, 17.1% for limbs ischemic disease and 23.6% for coronary heart disease. Occurrence of complications was associated with hypertension, duration of diabetes, dyslipidemia, microalbuminuria, 24-hour proteinuria, body mass index and HbA1c. Diabetic neuropathy was neither associated to HbA1c nor microalbuminuria.. HbA1c was conversely but not significantly associated with the number of DC realized. **Conclusion:** Conclusion: Vascular complications are considerably present in diabetes patients in the studied center, especially among those practicing less glycemic controls. Normalizing the level of HbA1c, controlling risk factors, and realizing DC may prevent the onset of vascular complications in DP.

**Pan African Medical Journal. 2013; 15:141. doi:10.11604/pamj.2013.15.141.2104**

This article is available online at: http://www.panafrican-med-journal.com/content/article/15/141/full

## Introduction

Considered as scarce in sub-Saharan region, cardiovascular diseases (CVD) are now the leading cause of mortality in some developing countries [1]. According to the World Health Organization (WHO), CVD account for 9.2% of total deaths in the Africa [2]. Various studies did provide evidence for an increasing burden of CVD in sub-Saharan region, with diabetes mellitus being the main contributor [3,4]. Changes in lifestyle and associated risk factors (obesity, dyslipidemia, hypertension and physical inactivity) increase the mortality of diabetes patients in sub-Saharan countries. The direct and indirect costs generated by prevention and treatment of diabetes complications are very important [5,6] and besides, micro and macrovascular complications of diabetes mellitus affect working-age people and then contribute to poverty in Africa [7,8]. In Africa, precarious conditions in management of diabetes and socio-economic difficulties are obstacles to achieve normoglycemia which is essential to prevent diabetic complications. The purpose of this study was to assess the prevalence of micro-and macrovascular complications, to identify various risk factors and their occurrence and to evaluate the role of a diabetic check-up in preventing these complications.

## Methods

In a retrospective part of the study, we reviewed clinical and laboratory records of diabetes patients (types 1 and 2) followed between 2000 and 2009 in the Endocrinology and Diabetology Unit of Douala General Hospital in Cameroon. We selected patients who made at least one diabetic check-up between 2000 and 2009 and excluded patients who didn't fit this criterion. Age of patients, duration of diabetes and medical history extracted from patient medical files were associated to laboratory data, recorded and analyzed. Clinical data recorded aimed at excluding cardiovascular morbidity. Particularly, we stressed to rule out history of chest pain consistent with angina, dyspnea, cardiac murmurs, and signs of heart failure. We also retrospectively evaluated echocardiographic features of patients in whom 2-D echo was performed. In the prospective part, an electrocardiogram (ECG) was performed on 121 patients using the CarTouch device (Cardionics SA, Brussels-Belgium).

**Diabetic check-up**

In Douala General Hospital, the diabetic check-up (DC) includes: endocrinology consultation (with clinical sensitivity assessment); ophthalmic consultation (visual acuity, Intra Ocular Pressure, slit lamp exam, funduscopy and angiography); dietary and nursing consultation (with blood pressure control and patient education); biological assessment (comprising glycemia, urea, creatinine, proteinuria, microalbuminuria); lipid profile (total cholesterol, HDL, LDL cholesterol and triglycerides) ; glycated hemoglobin (HbA1c)

**Diagnostic criteria**

All patients included in the study were treated and followed as out-patients in the Diabetology unit. Hypertension (HBP) was defined as diastolic blood pressure (BP) ≥85 mmHg and or systolic BP ≥130 mmHg (ANAES 2000). The diagnosis of coronary heart disease was retained if a patient reported typical angina pectoris or imaging techniques (2-D echo and/or ECG) displayed pathologic wall motion (akinesia or dyskinesia) by 2-D echo and/or Q waves in at least 2 adjacent leads by ECG. Peripheral artery disease was diagnosed using Leriche criteria. Dyslipidemia was defined according to the 2006 International Diabetes Federation (IDF) criteria: HDL cholesterol less than 0.4 g/L for men and 0.5 g/L for women; triglyceride level equal or greater than to 1.5 g/L and LDL cholesterol levels above 1.3 g/L was also considered. Diabetic nephropathy was assessed by a glomerular filtration rate (GFR, calculated with the MDRD formula) below 60 mL/min/1,73m$^2$ associated with positive 24 hours proteinuria. Peripheral neuropathy was assessed by clinical features associated with sensitivity examination including monofilament testing. Peripheral artery disease was diagnosed based on clinical symptoms and examination. Patients with organic chronic nephropathy were selected based on 24 hours proteinuria. In this study, the ALFEDIAM criteria of 1997 were used to classify diabetic retinopathy and HbA1c was determined using an enzymatic method. In summary, 249 check-ups were performed among 140 patients and the prevalence of each complication was calculated based on the first apparition of the diagnosis criteria.

**Statistical Analysis**

Statistical analysis was performed using the software Statview 5.0. (SAS Institute Inc., NC, USA). The Wilcoxon test was used for

comparison of means and the Spearman test for determination of association. A $p < 0.05$ was considered to be significant.

## Results

One hundred and forty DP out of 538 (26%) were finally included in this study; with 78(56%) men and 62(44%) women. The mean age was 55 ± 12 years (55 ± 10 years for men and 55 ± 15 for women). Sixty seven (47.8%) patients had at least one diabetes patient among their relatives. Type 2 diabetes accounted for 94.3% of cases. Diabetes prevalence was highest in patients aged between 50 and 59 years (39.3%). The various micro and macrovascular complications, their distribution by sex and their prevalence are respectively reported in **Table 1** and **Table 2**. Seventy percent of patients had at least one cardiovascular complication. **Table 3** shows the comorbidity analysis of complications.

**Diabetic retinopathy**

Retinopathy occurred after about 9 years of disease duration and was present in 33 (23.6%) patients. Mean age of patients with retinopathy was 58 ± 9 years; thirty two (96.9%) were type 2 diabetes patients. The diabetes duration was significantly higher in the group of patients with retinopathy compared to the group without retinopathy (13 ± 8 years versus 9 ± 5 years, $p = 0.02$). In 4 cases, retinopathy was present at the time of diagnosis. We found 63.6% limited non proliferative retinopathy including 9.5% of macular degeneration, 24.2% moderate non proliferative retinopathy, 3.1% preproliferative retinopathy and 9.1% minimal proliferative retinopathy.

**Diabetic nephropathy**

Thirty five (25%) patients developed diabetic nephropathy. All were type 2 diabetes. The mean delay for the onset of this complication was 8 years, their mean age was 62 ± 10 years and the mean duration of diabetes was significantly higher in the group of patients with nephropathy compared to the group without nephropathy (13 ± 7 years versus 9 ± 5 years, $p = 0.01$).

**Diabetic neuropathy**

Neuropathy appeared after 7 years and affected 56 (40%) patients. Their mean age was 56 ± 8 years, and all were type 2 diabetes. Diabetes duration was also significantly higher in this group compared to patients without neuropathy (12 ± 7 years vs 9 ± 5 years, $p = 0.0004$). Among these patients, 28.6% had lower limbs ischemic disease, 17.9% had foot trophic disorders and 12.5% lower limb edema.

**Coronary heart disease (CHD)**

CHD was found in 33(23.6%) patients out of whom 32 were type 2 diabetes. In these patients the mean age was 58 ± 9 years however, diabetes duration was not statistically different between patients with or without CHD (12 ± 7 years versus 9 ± 6 years, $p = 0.8$). Cardiac abnormalities were: left ventricular hypertrophy (45.5%), ECG-like myocardial ischemia (42.4%), ECG-two-D Echo-like myocardial infarction (27.3%) and left bundle branch block (3.1%).

**Lower limbs ischemic disease (LLID)**

This complication was found in 24 (17.1%) type 2 diabetes patients with a delay of onset of 7 years. Patient`s mean age was 60 ± 9 years and diabetes duration was not statistically different between subjects with and without LLID (12 ± 6 years versus 10 ± 6 years, $p = 0.6$). Diabetic foot was found in 16.4%: 65.2% of them had neuropathy associated to ischemic disease, 43.5% foot deformity and 13% wounds or ulcers. Their mean age was 58± 8 years and diabetes duration 15± 8 years.

**Stroke**

Patients in this group were all type 2 diabetes with a mean age of 57 ± 6 years. Stroke occurred after 6 years of disease duration. There was no difference in duration of diabetes in the groups of patients with or without history of stroke (8 ± 6 years versus 10 ± 6 years, $p = 0.3$). All patients were hypertensive.

**Risk Factors**

Several risk factors for CVD were associated with the occurrence of these complications. **Table 4** shows the distribution of risk factors associated to micro and macroangiopathy. Sixty four percent of

patients nephropathy with also presented retinopathy; these two complications were significantly associated (r = 0.5, p <0.0001).

**Effect of diabetic check-up**

We found positive correlation between the number of diabetic check-up performed and the number of complications detected(r = 0.3, p<0.0001). Negative but not significant correlation were found between HbA1c and the number of HbA1c assay performed (r = - 0.022, p = 0.6) on the one hand and the number of diabetic check-up (r = - 0.055, p = 0.5) on the other hand.

## Discussion

In Cameroon retinopathy is the most explored microvascular complication its prevalence is around 37% [9, 10]. Our study did find a prevalence of 23.6% which is lower than the previous reports in Cameroon, nevertheless within the range of 7-50% reported by several African authors [11-13]. Despite the fact that our study was mostly based on angiography and the other on funduscopy, we can explain the difference by the benefit of the implementation of a national program which aimed to reduce the prevalence of diabetes complications. In addition, the ophthalmologic check-up we realized included fundoscopy and angiography which is recommended by some authors [14]The value and importance of our check-up for screening and preventing diabetic retinopathy has been reinforced by this recommendation.

Studies on diabetic nephropathy in Africa reported various rate of prevalence. Some indicated lower rates than our: 11.6% in Sudan and 17.1% in Uganda [15, 16]; while others found similar results: 22% [18]. Djrolo et al. [18] found that diabetic nephropathy was less common than retinopathy (28% versus 51%). These results are in concordance with those of Crini et al. [19] with a prevalence of 23% versus 57%, however, differ from the present study where the prevalence of nephropathy and retinopathy were almost similar (25% versus 23.6%).

Regarding neuropathy, the prevalence we found is in agreement with another studie conducted in Africa [17] but differs from occidental studies [20]. Although neuropathy is a consequence of chronic hyperglycemia, we did not find a significant association between neuropathy and HbA1c. This may be due to the fact that clinical evaluation is based on subjective criteria such as paresthesia which is enhanced by any type of glucose fluctuations (unstable blood sugar levels or hypoglycemia).

Concerning macrovascular complications, this study found that coronary disease was the most frequent (23.6%). Elbagir et al. [17] find concurrent results with a prevalence of 28% for CHD, 10% LLID and 5.5% stroke. In sub-Saharan Africa, the prevalence of LLID range between 1.7 and 28% [21-23]; the prevalence we found (17.1%) is within these limits. We do understand that 67% of patients with LLID had diabetic foot due to the pathophysiologic role of ischemia. The prevalence of diabetic foot we found is in agreement with the retrospective study of Sano et al. [24] in Burkina Faso (18.9%). In our study, the mean age of patients with diabetic foot was higher than that found by Sano et al (58 years versus 53 years). However, this mean age reported by African authors remains lower than European studies, which ranged from 63 to 73 years [25-27]. This highlights the thorny problem of diabetic foot prevention in Africa compared to developed countries where the quality of care delays the onset of this complication responsible for 70% of amputations in diabetes patients [28]. Risk factors identified in this study were also reported by several authors and a recent study showed that occurrence of complications was significantly associated with reduced physical activities [29].

Microalbuminuria is an independent risk factor for cardiovascular morbidity and mortality in type 1 and type 2 diabetes [30]. It is also known to be an independent marker of cardiovascular risk [31] which decreases with increased physical activities [32, 33]. Perkovic et al. [34] found a positive association between proteinuria and coronary disease as we did. However, the association of retinopathy with microalbuminuria remains quite controversial. Some studies, in agreement with ours, found a significant association between microalbuminuria and retinopathy [35-37] while others reported opposite results [38-39].

Several studies [40-43] described dyslipidemia as risk factors for CHD. It's prevalence in Cameroon is 43% [43]. Bieleli [44] shows that diabetes patients with stroke have a lipid profile (low HDL and high LDL) significantly different from the one in diabetes patients without stroke. Other recent studies showed that elevated LDL and triglycerides were associated with severe diabetic retinopathy suggesting that dyslipidemia may favor the onset or progression of retinopathy [45].

In our sample of patients with type 2 diabetes, 44.3% were in overweight and 30% were obese. Epacka et al. [46] showed that BMI was inversely correlated with sport and physical activities (SPA) in Cameroon. This suggests the emergence of other lifestyle risk factors already incriminated by other authors in Cameroon [48] such as dietary habit and physical inactivity in relation with reduced SPA. Those factors inducing insulin resistance can lead to diabetes complications.

The non-significant but negative association we found between HbA1c and the number of annual diabetic check-up suggests that we could reduce or at least stabilize the HbA1c with regular check-ups. The lack of significance could be explained by the irregular dosage of HbA1c. In fact, over 60% of our sample realized less than 20% of HbA1c dosage of what was expected. Positive correlation found between complications and the number of diabetic check-up means that each time check-up was made, complications were found. This shows the efficiency check-up in the screening of complications. However, prevention of complications by implementing diabetic check-up remains to be confirmed by a prospective study. In our sample over 55% of patients made only one diabetic check-up. In addition, the mean time between two check-ups was 3 years and might be enough long to develop complications. The non-compliance can be due to high cost and reduced access to care and can explain the lack of significance of the association between HbA1c and the number of check-up. Thus, this study shows the importance of diabetic check-up in terms of screening for complications; however it does not assess its contribution in preventing of microvascular and macrovascular complications. Further studies are needed to be conducted on this topic.

**Study limitations**

Although this study looks original and enrolled a consistent sample, some limitations need to be underlined. First, the missing of some data due to the retrospective aspect of the study; second, the low rate of recommended tools for accurate diagnosis of diabetes complications may influence or results.

## Conclusion

Vascular complications are especially important in type 2 diabetes patients in the General Hospital of Douala who are practicing less glycemic controls. Various risk factors have been identified as associated to the occurrence of these complications. Diabetic check-up has not yet confirmed its benefit in term of prevention of complication but we think that a regular realization may give better results. Normalizing HbA1c, controlling risk factors, and realizing DC may prevent the onset of vascular complications in diabetes patients.

## Competing interests

The authors declared they have no competing interests.

## Authors' contributions

S Moumbe Tamba and S.H. Mandengue are main investigators; M. Epacka Ewane, analysed the Diabetology aspects ; A Bonny Bonny, analysed the ECG and Cardiology aspects ; C. Nkidiaka Muisi, E.Nana, A. Ellong, C. Ebana Mvogo, contributed in the analysis of Ophthalmology aspects. All the authors have read and approved the final version of the manuscript.

## Acknowledgments

We are grateful to the Douala General Hospital, for the authorization to conduct this study in its Endocrinology and Diabetology unit.

## Tables

**Table 1**: distribution of microvascular complications

**Table 2**: Distribution of macrovascular complications

**Table 3**: Comorbidity

**Table 4**: Risk factors associated with micro and macroangiopathy

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**Table 1**: distribution of microvascular complications

| | **microangiopathies** | | | | | |
|---|---|---|---|---|---|---|
| | **retinopathy** | | **nephropathy** | | **neuropathy** | |
| | **effective** | **percent (%)** | **effective** | **percent (%)** | **effective** | **percent (%)** |
| **men** | 19 | 57.6 | 11 | 31.4 | 33 | 58.9 |
| **women** | 14 | 42.4 | 24 | 68.6 | 23 | 41.1 |
| **total** | 33 | 100 | 35 | 100 | 56 | 100 |
| **prevalence** | 23.6% | | 25% | | 40% | |

**Table 2**: Distribution of macrovascular complications

| | Macroangiopathies | | | | | |
|---|---|---|---|---|---|---|
| | Coronary heart disease (CHD) | | Lower limbs ischemic disease (LLID) | | Stroke | |
| | Effective | Percent (%) | Effective | Percent (%) | Effective | Percent (%) |
| Men | 20 | 60.6 | 11 | 45.8 | 5 | 71.4 |
| Women | 13 | 39.4 | 13 | 54.2 | 2 | 28.6 |
| Total | 33 | 100 | 24 | 100 | 7 | 100 |
| Prevalence | 23.6% | | 17.1% | | 5% | |

**Table 3**: Comorbidity

| Number of complications | Subjects affected | |
|---|---|---|
| | n | % |
| 2 | 38 | 27,1 |
| 3 | 18 | 12,9 |
| 4 | 4 | 2,9 |
| 5 | 3 | 2,1 |
| 6 | 0 | 0,0 |

**Table 4**: Risk factors associated with micro and macroangiopathy

| | Retinopathy | | Nephropathy | | Neuropathy | | CHD | | LLID | | Stroke | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | r | p | r | p | r | p | r | p | r | p | r | p |
| HbA1C | 0.3 | 0.0003 | 0.2 | 0.03 | 0.03 | 0.7* | 0.2 | 0.004 | 0.3 | 0.0002 | 0.4 | < 0.0001 |
| High blood pressure | 0.5 | < 0.0001 | 0.5 | < 0.0001 | 0.4 | < 0.0001 | 0.4 | < 0.0001 | 0.6 | < 0.0001 | 0.7 | < 0.0001 |
| Dyslipidemia | 0.3 | 0.0008 | 0.3 | 0.005 | 0.3 | 0.0004 | 0.4 | < 0.0001 | 0.5 | < 0.0001 | 0.6 | < 0.0001 |
| Diabetes duration | 0.5 | < 0.0001 | 0.3 | 0.0002 | 0.4 | < 0.0001 | 0.3 | 0.0002 | 0.5 | < 0.0001 | 0.4 | < 0.0001 |
| BMI | 0.2 | 0.01 | 0.2 | 0.007 | 0.1 | 0.09 | 0.3 | 0.001 | 0.4 | < 0.0001 | 0.5 | < 0.0001 |
| Microalbuminuria | 0.3 | 0.0003 | 0.2 | 0.01 | 0.1 | 0.1* | 0.3 | 0.0006 | 0.4 | < 0.0001 | 0.5 | < 0.0001 |
| Proteinuria | 0.8 | < 0.0001 | 0.7 | < 0.0001 | 0.7 | < 0.0001 | 3 | 0.0006 | 0.7 | < 0.0001 | 0.8 | < 0.0001 |
| (*): Not significant; BMI = Body Mass Index | | | | | | | | | | | | |