EPIDEMIOLOGICAL ASPECTS OF DIABETES IN CAMEROON:
WHAT IS THE ROLE OF TROPICAL DIABETES?

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SUMMARY - Diabetes is a worldwide public health problem made more acute in Africa by low socio-economic standards. Cases with an unusual clinical course are frequent and probably related to tropical diabetes, a syndrome that has not yet been precisely defined. This study reports the results of a prospective study carried out in Cameroon on 550 diabetic patients attending the Yaounde Central Hospital who were followed between December 1990 and July 1994. They were classified according to WHO criteria into 136 insulin-dependent diabetes mellitus (IDDM) (24.7 %), 405 non-insulin-dependent diabetes mellitus (NIDDM) (73.7 %) and 9 diabetes secondary to other diseases (1.6 %). No cases of malnutrition-related diabetes mellitus (MRDM) were found, but 18 subjects were considered to have so-called “African diabetes”. Investigation of the cohort showed epidemiological and clinical features markedly different from those of Caucasian diabetic subjects. The age of onset in IDDM occurred in all age groups, with a mean (± SD) close to that of NIDDM (40.9 ± 4.8 years vs 49 ± 10.9 ; P < 0.001). A clear male preponderance was found (M/F sex ratio = 1.63), as it has been reported in most studies from sub-Saharan Africa, in contrast with the slight female predominance noted in the Sahel and Saharan countries. An increased prevalence of young and non-obese NIDDM was also found. Seventy-nine NIDDM cases (19.5 %) were detected in individuals under 40 years of age, including 31 with normal weight. Many atypical features were noted: IDDM in obese patients, NIDDM in ketotic subjects and patients with varying insulin requirements, all of which led to difficulties in classifying many diabetic patients according to current practices. All these uncommon features are concordant with the nature of tropical diabetes, including not only MRDM but also African diabetes which occurs in individuals older than MRDM patients who show no signs of malnutrition. Thus, tropical diabetes is apparently a syndrome with aetiological heterogeneity which requires further definition through clinical, genetic and immunological studies. Diabetes & Metabolism 1997, 23, 61-67.

Key-words: diabetes, epidemiology, tropical diabetes, Cameroon.

RÉSUMÉ - Aspects épidémiologiques du diabète au Cameroun. Quelle est la place du diabète tropical ? Le diabète pose un réel problème de santé publique dans le monde. En Afrique la prise en charge du diabète est compliquée par les difficultés socio-économiques. Des modalités évolutives atypiques paraissent fréquentes dans l’ensemble des pays tropicaux, mais sont encore mal précisées. Nous rapportons les résultats d’une étude prospective concernant 550 diabétiques suivis au Cameroun entre décembre 1990 et juillet 1994. La classification révèle 136 DID (24.7 %), 405 DNID (73.7 %) et 9 diabètes secondaires (1.6 %). Aucun cas de diabète sucré lié à la malnutrition (DSLM) n’a été mis en évidence mais nous avons relevé 18 sujets (3 %) correspondant aux critères du « diabète africain ». L’étude de cette population de diabétiques montre des particularités qui les différencient des séries occidentales. L’âge de révélation du DID est dispersé dans toutes les tranches d’âge avec une moyenne à 40,9 ± 14,8 ans proche de la moyenne de découverte du DNID à 49 ± 10,9 ans. Le sex-ratio est à 1,63 révélant une nette prédominance masculine quel que soit le type de diabète. Il existe aussi une fréquence accrue de DNID jeunes non obèses. On observe des cas d’évolution atypique avec fluctuation du besoin insulinique rendant la classification difficile. Enfin la prévalence de l’obésité chez les DNID est plus faible qu’en Occident. Toutes ces observations vont dans le sens de l’existence du diabète tropical dont la réalité ne se résume pas au DSLM. Le diabète africain est un autre aspect de ce diabète tropical, mais ses critères actuels ne permettent pas de regrouper toutes les formes particulières à l’Afrique qui paraissent d’une grande hétérogénéité sur le plan étiologique. Diabetes & Metabolism 1997, 23, 61-67.

Mots-clés: diabète, épidémiologie, diabète tropical, Cameroun.

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Diabetes in African Blacks may constitute an entity with specific features and a peculiar disease course. The high frequency and the severity of complications in these patients have been noted by many authors and appear to be largely due to inadequate medical care related to poor socioeconomic standards. Another major problem concerns difficulties in classifying patients in Africa. In a recent paper [1], Alberti considered problems in the definition of Type 2 diabetes relative to the exclusion of other types. Inevitably, non-insulin-dependent diabetes mellitus (NIDDM) constitutes a heterogeneous group of aetiologic disorders. However, the problem in Africa seems to be much more complex since intermediate forms of diabetes have been described in young adult patients with normal weight and great variability in ketosis and insulin need [2]. Several authors have previously tried to define the characteristics of "tropical diabetes", a recognized form whose characteristics remain largely unclear [3-8]. The purpose of this study was to report the features of diabetic patients from Cameroon and to define the nature of atypical forms of diabetes in African people and the relations with tropical diabetes.

## PATIENTS AND METHODS

The survey was conducted at the Central Hospital of Yaounde in Cameroon (Central Africa). A total of 550 diabetic subjects were selected and followed among inpatients and outpatients from December 1990 to July 1994.

### Parameters studies

Data were obtained for individual characteristics (age, gender, ethnic group, usual living place and initial reason for hospital admission (inpatient or outpatient), supposedly related to the degree of severity of diabetes): a family history of diabetes; the patient’s own history of diabetes (date and circumstances of diabetes detection, length of follow-up, changes in classification, reasons for leaving the study); height and maximum and present weight; and fasting glycaemia, post-eating glycaemia and urinary ketosis.

### Criteria for diabetes classification

The diagnosis and classification of diabetes were based on currently used WHO criteria as revised by the World Health Organization Expert Committee in 1985 [9]. A subject was considered diabetic if fasting glycaemia in two venous plasma determinations was ≥ 140 mg/dl (or ≥ 120 mg/dl for capillary whole blood with test strips), or the casual whole blood glucose level was ≥ 200 mg/dl. Five groups of diabetic patients were defined:

1. Insulin-dependent diabetes mellitus (IDDM) was considered to be present when classical symptoms of diabetes were associated with highly elevated glycaemia and profuse ketone bodies in urine. Age and corpulence were not taken into account.
2. A group designated as diabetes due to other diseases included all patients affected by chronic calcific pancreatitis (diabetes associated with chronic greasy diarrhea and/or pancreatic calcifications) or diseases increasing insulin-resistance, such as acromegaly and Cushing's syndrome, or treatment with corticosteroids.
3. Malnutrition-related diabetes mellitus was defined on the basis of the criteria proposed by Ahuja [3,4]: a history of malnutrition in childhood, age of onset before 30 years, body mass index (BMI) < 19 kg/m², insulin-requiring treatment, no tendency to develop ketosis even when insulin therapy is interrupted. Pancreatic calcifications were not constant. At least 2 subtypes of this form exist: fibrocalculous pancreatic diabetes with calcifications, mainly observed on the Indian subcontinent, and the J-type (initially reported in Jamaica) without calcification, which seems to be more frequent in Africa.
4. Gestational diabetes applied only to women whose diabetes was first detected during pregnancy.
5. Non-insulin-dependent diabetes mellitus (NIDDM) included all patients not classified in one of the preceding groups.

This classification system has the advantage of being based on simple WHO criteria, which theoretically allow valid comparisons to be made between all the studies which have adopted them. Yet the use of this system is obviously questionable insofar as many criteria are not taken into account, such as age of onset, weight, or genetic and immunologic markers. However, it is not yet possible to integrate all of these parameters into a system, which would require the inclusion of many unclassifiable subgroups that have no place in the current classification scheme. Moreover, the high cost of biological markers generally prevents their use in epidemiological studies in developing countries. Nonetheless, diabetes classification needs to be clarified in order to include specific forms of the disease that can be seen in tropical countries and more precisely in Africa. Therefore, we attempted to identify other subgroups than those included in the WHO classification which could correspond to clinical or pathogenic entities.

The most recognized type is Maturity Onset Diabetes of the Young (MODY), whose genetic aetiology is now well established (disease is most often due to a mutation of the glucokinase gene). In this study, the criteria for MODY were those proposed by Tattersall and Mansell [10], i.e. diabetes diagnosed before the age of 25 and treatable without insulin for more than 5 years.

Malnutrition-related diabetes mellitus is not frequent in Africa, but another subgroup of tropical diabetes has been described whose criteria, as defined by Cuisinier-Raynal et al. (6), are diabetes onset between 20 and 39 years, normal or low weight (BMI ≤ 23 for male and ≤ 25 for female), a low standard of living, low ketosis-prone status and no requirement for insulin treatment.

In addition to this classification scheme, we took into account the notion of the insulin-treated diabetic patient considered in some studies. All patients receiving insulin, regardless of their type of diabetes and the reason for this treatment, were considered to be insulin-treated.

### Criteria for obesity

Fatness was evaluated by the BMI, which was calculated by the weight/height² (kg/m²) ratio. Those individuals were considered obese whose BMI was ≥ 25 in females and ≥ 27 in males. Subjects whose BMI was < 23 in females and
< 25 in males were considered normal or lean. Those whose BMI was between these limits were considered moderately overweight but not obese.

**Statistical analysis** – Qualitative variables were analysed by the chi-square or Fisher exact test, depending on cell sizes. Mean comparisons were determined by Student’s *t*-test and analysis of variance. All tests were performed for a statistical alpha risk ≤ 0.05.

### RESULTS

#### Classification

As results relative to WHO criteria were likely to change with time, we evaluated the classification for each patient 3 times: at diabetes onset, at inclusion in the study and at the time of leaving the study. Table I shows the results for this procedure. In this population, we found 382 subjects (69 % of the total number) whose diabetes was known before the study and whose first classification was done by anamnesis, thus not always with certainty. For this reason, 3 patients could not be classified. At the end of follow-up, the distribution of patients was 136 IDDM (24.7 %), 405 NIDDM (73.7 %) and 9 diabetes caused by other diseases (1.6 %). As this end-of-follow-up classification was more reliable, it was adopted as the sole basis for analysis of results.

#### Table I. Changes in classification during study.

<table>
<thead>
<tr>
<th>Classification at onset</th>
<th>Classification at inclusion</th>
<th>Classification at the end of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>IDDM</td>
<td>98 (17.9)</td>
<td>134 (24.4)</td>
</tr>
<tr>
<td>NIDDM</td>
<td>442 (80.4)</td>
<td>408 (74.2)</td>
</tr>
<tr>
<td>Other types</td>
<td>7 (1.3)</td>
<td>8 (1.4)</td>
</tr>
<tr>
<td>Not evaluated</td>
<td>3 (0.5)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

The aetiologies of secondary diabetes were: 1 case of Cushing’s syndrome, 2 cases after corticosteroid treatment and 6 cases of chronic calcific pancreatitis, all with chronic alcoholic intoxication. No cases of malnutrition-related diabetes mellitus or gestational diabetes were found in this series. Three patients presenting with MODY features represented 0.5 % of the total cohort and 0.7 % of the 405 NIDDM. Among these 3 subjects (2 men and 1 woman), only one had known familial diabetes; their mean BMI was 19 kg/m².

Eighteen subjects met the criteria for African diabetes, representing 4.4 % of the 405 NIDDM and 22 % of the subjects whose NIDDM was discovered before the age of 40 years. The distribution (14 males and 4 females) showed a large male predominance (sex ratio 3.5). Mean age at onset was 33.5 ± 5 years, and mean BMI was 20.8 kg/m².

A few patients with an atypical course of diabetes could not be included in these different categories. Four obese diabetic subjects (1 male and 3 females), whose BMI was 30 kg/m², were considered IDDM since they presented strong ketosis (and even ketoacidosis in one case) associated with a high blood glucose level, severe asthenia and insulin-requiring diabetes. Twelve other patients with high glycaemia and ketosis were considered as NIDDM because they recovered a normal blood glucose level with ketosis regression within a week’s time. Glycaemic control was then maintained in subsequent months. Contrary to the therapy followed by the former group, these patients did not receive insulin treatment immediately because of their obesity (mean BMI: 30 kg/m²) and good physical condition.

#### Age

Mean age at diabetes onset was 46.9 ± 12.5 years (Table II). In terms of diabetes type, the age was 40.9 ± 15 years for IDDM and 48.9 ± 10.8 years for NIDDM, showing a significant difference (*P* < 0.001). The distribution of diabetic patients according to category and ten-year age groups is indicated in Figure 1. It is noteworthy that IDDM occurred at any age and that only 53 % of cases were revealed before 40 years. NIDDM was also detected at any age. In both types of diabetes, maximal onset frequencies were found in middle age: in the fourth decade (31-40 years) in IDDM and the fifth decade (41-50 years) in NIDDM. At the end of follow-up, overall mean age was 53.2 ± 12.8 years. No significant difference was found between males (53.1 ± 13 years) and females (54 ± 12.5).

#### Table II. Age at diabetes onset.

<table>
<thead>
<tr>
<th>Diabetes type</th>
<th>Number</th>
<th>m ± SD* (years)</th>
<th>Limits (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDDM</td>
<td>136</td>
<td>40.9 ± 15</td>
<td>14-72</td>
</tr>
<tr>
<td>NIDDM</td>
<td>405</td>
<td>48.9 ± 10.8</td>
<td>19-78</td>
</tr>
<tr>
<td>Other types</td>
<td>9</td>
<td>46.5 ± 12</td>
<td>29-64</td>
</tr>
<tr>
<td>Total</td>
<td>550</td>
<td>46.9 ± 12.5</td>
<td>14-78</td>
</tr>
</tbody>
</table>

* m ± SD: mean ± standard deviation.

#### Sex

The distribution of patients by gender is given in Table III. The overall male/female sex ratio was 1.63,
with no statistically significant difference between the two types of diabetes. A significant difference was found \((P = 0.015)\) between outpatients \((SR = 1.95)\) and inpatients \((SR = 1.27)\).

**Place of residence** – Among the study population, 420 individuals \((76.6\%)\) were living in Yaounde, the capital of Cameroon, and 114 \((20.7\%)\) outside the town, sometimes quite far away. Information on the usual place of residence was not obtained from 3 \(\%\) of patients.

**Mode of hospital admission** – For the 550 patients attending the Central Hospital of Yaounde and included in the study, 225 \((41\%)\) were inpatients and 325 \((59\%)\) outpatients at the first visit. IDDM subjects represented 34.2 \(\%\) of inpatients vs 18.9 \(\%\) of outpatients; the difference was highly statistically significant \((P = 0.00006)\).

**Body mass index** – The overall mean BMI in this population was 24.4 \(\pm\) 4.8 kg/m\(^2\), with a significant difference \((P < 0.001)\) between IDDM \((21.6 \pm 4)\) and NIDDM \((25.4 \pm 4.7)\). Using defined criteria for obesity, we found that 44 \(\%\) NIDDM had normal or low weight, 17 \(\%\) moderate overweight and 39 \(\%\) obesity. There was a strong sex difference in obese NIDDM \((27.5 \%\) of men vs 58.5 \(\%\) of women; \(P < 0.001)\). Moreover, taking into account those cases in which previous obesity could be determined, the prevalence of obesity (present or past) was found in 60 \(\%\) of NIDDM subjects.

**Family history of diabetes** – A family history of diabetes was found in 26.5 \(\%\) of IDDM vs 26.7 \(\%\) of NIDDM (difference not statistically significant). It is noteworthy that many subjects could not provide reliable information on this point. Many, in fact, had never heard about diabetes. Thus, it is likely that these results underestimate the true prevalence.

**Ethnic groups** – The ethnic distribution of diabetics is given in Table IV according to type of diabetes. The Bamileke ethnic group appears to be predominant, although no conclusion can be drawn since no statistics were available on ethnic distribution in the total population of Yaounde.

**Mode of presentation** (Table V) – It is noteworthy that for more than half of the individuals diabetes was...
détectées par l'expression d'un symptôme classique ou de signes de la maladie. Les polydipsies et polyuries, ainsi que la perte de poids, étaient rapportées chez 290 patients (52.7 % du total). La perte de poids était fréquemment associée à polyurie, mais les patients n'étaient pas toujours capables de déterminer combien de poids ils avaient perdu. Il n'y avait pas de différence significative fondamentale, retrouvée, selon le type de diabète.

**Diabète de type 1 (IDDM)**

- Les diabétiques de type 1 étaient définis par l'insulinodépendance à l'inclusion dans l'étude, avec un âge de malignité dans une tranche entre 7 et 12 mois. Dans cette tranche, on a observé 18 patients correspondant à un diabète de type 2 avec un rapport de stade insulino-dépendant et de stade non insulino-dépendant. La proportion de patients insulinodépendants était de 6.7 % au terme de la suivi. Parmi les 134 IDDM à l'inclusion, 9 patients (6.7 %) ont perdu leur dépendance insulinique. Parmi les 134 IDDM à l'inclusion, 9 patients (6.7 %) ont perdu leur dépendance insulinique.

**Diabète de type 2 (NIDDM)**

- Les diabétiques de type 2 étaient définis par l'apparition de signes clairs de diabète de type 2 après l'inclusion dans l'étude, avec un âge de malignité dans une tranche entre 7 et 12 mois. Dans cette tranche, on a observé 18 patients correspondant à un diabète de type 2 avec un rapport de stade insulino-dépendant et de stade non insulino-dépendant. La proportion de patients insulinodépendants était de 6.7 % au terme de la suivi. Parmi les 134 IDDM à l'inclusion, 9 patients (6.7 %) ont perdu leur dépendance insulinique. Parmi les 134 IDDM à l'inclusion, 9 patients (6.7 %) ont perdu leur dépendance insulinique.

**Discussion**

Il est clair que les critères proposés pour la classification du diabète par les WHO ne sont pas suffisamment précis et spécifiques pour permettre une intégration de la plus récente connaissance sur l'âge du diabète. Cependant, ils ont l'avantage d'être simples et coûts-efficaces, permettant un bon gestion de la maladie diabétique que ce soit dans les pays en développement ou en développement. En effet, les maladies ne sont pas toujours un diagnostic de routine, mais nécessitent une prise en charge adéquate. Les maladies diabétiques sont classées par la classification de l'OMS, mais ces critères ne sont pas toujours identiques. Cependant, les définitions proposées par les WHO ne sont pas suffisamment précises pour déterminer une classification homogène aétologique. En effet, il est difficile de définir les différents types de diabète de manière cohérente. Il est donc nécessaire de prendre en compte les facteurs environnementaux et génétiques qui peuvent influencer la classification du diabète.

Il est également important de prendre en compte les changements de classification qui se produisent avec le temps. Ces changements ne sont pas constants et peuvent être influencés par de nombreux facteurs, tels que la prise en charge médicale ou les modalités de suivi. Il est donc nécessaire de prendre en compte ces changements lors de la classification du diabète.

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ported. Therefore, tropical diabetes appears to be much more heterogeneous than might be expected.

The classical notion that IDDM occurs in young people and NIDDM in maturity is not true in Africa where diabetes of both types affects people of all ages. This fact has been reported by Swai et al. in East Africa [21] and Gill and Huddle in South Africa [27]. Indeed, the present work shows that the mean age at diabetes onset was significantly lower in IDDM than NIDDM (40.9 vs 48.9 years) (Table 2). However, it must be emphasized that the difference of age at onset between the two types is not great and that mean age at onset for IDDM is surprisingly elevated (40.9 ± 15 yrs), which can be explained by the fact that 48.5 % of IDDM are revealed after 40 years of age. It may be objected that we had no islet cell antibody determination to prove that patients classified as IDDM were certainly Type 1. Moreover, age at onset in Type 1 could have been high because diagnosis was delayed. Yet it seems quite unlikely in a medically equipped town such as Yaounde that an NIDDM patient whose disease had developed to a stage of beta-cell failure with ketosis would be detected at a first hospital visit. Who can reasonably suppose that diagnosis could be delayed for ten years or more in a patient with IDDM ? Conversely, we found 79 NIDDM (19.5 % of total NIDDM) whose onset was before 40 years of age and who were still non-insulin-dependent after 2 years, with a mean diabetes duration at the end of the study of 8.4 ± 6.6 years. All these arguments offer evidence for the spreading and overlapping of onset ages of the two main aetiologic types of diabetes, as is clearly indicated in Figure 1.

The results reported here show an evident male preponderance, with an overall male/female sex ratio (SR) of 1.63. Such an excess of diabetic men has been reported in most African studies: 1.48 in Gabon [15], 1.86 in Togo [13], 2.32 in Tanzania [21], 2.33 in Cameroon [20] and 2.8 in Ivory Coast [22]. However, several works conducted in the Sahel or Saharan region have reported a slight female predominance: 0.78 in Senegal [14], 0.79 in Mauritania [17], 0.97 in Mali [19] and 0.99 in Ethiopia [16]. This male predominance could be due to lesser access to medical care for women for social or cultural reasons. In our study, the lower SR (1.27) among inpatients supported this hypothesis since it is understandable that the difference between men and women in requesting medical markers.

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Obesity is an important risk factor in diabetes in Africa as everywhere else in the world, but its prevalence is lower than in Europeans. In our study, 39 % of NIDDM were obese at inclusion and 60 % had a history of obesity. Thus, the prevalence of obesity for Central African NIDDM is intermediary between that of Western countries, where the rates are in the 50-80 % range [31] and that of Sahel countries where the rates are 23 % in Burkina Faso [32], 24.7 % in Ethiopia [16] and 35.5 % among men in Mauritania [17]. In the last case, the problem is more complex. In Mauritania, the overall prevalence of obesity among NIDDM has been estimated at 60 %, but a high sex difference was found (35.5 % in men vs 75.5 % in women) [33]. There is in fact a cultural reason for the high prevalence of female obesity in Mauritania. In the Moorish ethnic group, obesity is a traditional determinant of female beauty and is obtained by force-feeding girls with camel milk.

In conclusion, this prospective study in a cohort of African diabetes shows the difficulties in classifying patients according to WHO criteria. The presence of ketones in urine, in association with high glycaemia, is not a reliable criterion for determining insulin-dependency in Type 1 diabetes or for predicting the patient’ long-term insulin needs. Although the concept of “tropical diabetes” remains unclear, it must be emphasized that certain characteristics, i.e. age of onset, sex and fatness, are different in Africa than in Western countries. Otherwise, we found a few cases of diabetes with an atypical clinical course, and several others authors have reported similar cases. Thus, many findings indicate that some cases of diabetes in Africa have certain peculiarities and an evident aetiologic heterogeneity. Further epidemiological studies are needed, particularly including genetic and immunological markers.

REFERENCES


