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REVIEW

DIABETES IN AFRICANS

Part 1: epidemiology and Clinical Specificities

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SUMMARY - The prevalence of diabetes in African communities is increasing with ageing of the population and lifestyle changes associated with rapid urbanisation and westernisation. Traditional rural communities still have very low prevalence, at most 1-2%, except in some specific high-risk groups, whereas 1-13% or more adults in urban communities have diabetes. Type 2 diabetes is the predominant form (70-90%), the rest being represented by typical type 1 patients and patients with atypical presentations that require more pathophysiological insight. Due to the high urban growth rate, dietary changes, reduction in physical activity, and increasing obesity, it is estimated that the prevalence of diabetes is due to triple within the next 25 years. In addition, long-term complications occur early in the course of diabetes and concern a high proportion of patients, probably higher than in other ethnic groups, and that could be partly explained by uncontrolled hypertension, poor metabolic control and possible ethnic predisposition. The combination of the rising prevalence of diabetes and the high rate of long-term complications in Africans will lead to a drastic increase of the burden of diabetes on health systems of African countries. The design and implementation of appropriate strategy for early diagnosis and treatment, and population-based primary prevention of diabetes in these high-risk populations is therefore a public health priority.

Key-words: diabetes, Africa, prevalence, complications.

RÉSUMÉ - **Diabète chez l'africain : Partie 1 : épidémiologie et caractéristiques cliniques :** La prévalence du diabète dans les communautés africaines augmente avec le vieillissement de la population et les modifications du mode de vie en rapport avec une occidentalisation et une urbanisation rapide. Les communautés traditionnelles rurales gardent une prévalence très basse inférieure à 1-2 % excepté dans certains groupes à haut risque, alors que 1 à 13 % voir plus des adultes vivant dans les communautés urbaines ont un diabète.
Le diabète de type 2 est la forme prédominante (70 à 90 %), le reste étant représenté par le diabète de type 1 et les patients ayant une forme atypique de diabète qui nécessite d'être élucidée. Compte tenu de la forte croissance urbaine, des modifications alimentaires, de la réduction de l'activité physique et de l'augmentation de l'obésité, la prévalence du diabète devrait tripler dans les 25 prochaines années. De plus les complications chroniques apparaissent précocement dans l'évolution du diabète et concernent une forte proportion de patients, probablement plus élevée que celle observée dans d'autres groupes ethniques, ce qui pourrait être en partie expliquée par une hypertension artérielle mal contrôlée, un mauvais contrôle glycémique et des prédispositions génétiques. L'association de l'augmentation de la prévalence du diabète et de la forte proportion des complications chroniques chez l'africain vont entraîner une augmentation considérable des coûts du diabète dans les systèmes de soins des pays africains. La mise en place de stratégies appropriées pour le diagnostic et le traitement précoce associés à un programme de prévention primaire du diabète dans ces populations à haut risque représente donc une priorité de santé publique.

Mots-clés : diabète, Afrique, prévalence, complications.

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The prevalence of diabetes mellitus and other non-communicable diseases is on the rise in African communities due to the ageing of the population and drastic lifestyle changes accompanying urbanisation and westernisation [1]. Diabetes is no longer rare, and is higher in populations of African origin who have migrated to Western countries compared to Caucasians living in the same countries [2]. Type 2 diabetes is the predominant form, yet, a classification problem persist for a high proportion of the patients [3, 4]. There are numerous reports in populations of African ancestry, of clinical presentations of diabetes, which do not easily fit with the definition criteria of the main known types. Apart from classical type 1 and type 2 diabetes, tropical diabetes and ketosis-prone atypical diabetes have been described [5]. Moreover, diabetes mellitus is associated with a high rate of long-term complications in populations of African origin. Therefore, it will represent a growing burden of health care systems of African countries, most of which already face difficult economic conditions. However, a prospective approach of this burden and possible prevention strategies has been hindered by the scarcity of data on diabetes in Africa. Thus, we aimed to review available evidence on the epidemiology and clinical specificities of diabetes in Africans.

■ EPIDEMIOLOGY OF DIABETES

Prevalence and incidence

Over the past century, diabetes mellitus has been considered as a rare medical condition in Africa, as illustrated by the famous statement of Dr Cook who wrote "... diabetes is very uncommon but very fatal..." in his 1901 notes on the diseases met in Africa [6]. However, epidemiological studies carried out in the last decade of the 20th century have provided evidence of a different picture. There is a global trend towards the increase of the incidence and prevalence of diabetes mellitus in African populations [7]. Indeed, Africa is experiencing one of the most rapid demographic and epidemiological transition of the world history [8]. It is characterised by a tremendous rise in the burden of non communicable diseases, underlined by the increasing life expectancy and lifestyle changes resulting from the reduction of infectious diseases and fertility, and the westernisation [8, 9].

Almost all the reports published between 1959 and 1985 showed a prevalence of diabetes ≤ 1.4%, except those in the Republic of South Africa where up to 3.6% prevalence was reported [10-14]. The rural areas had the lowest prevalence, around 0 to 0.5% [10-14]. Across country comparison is however difficult due to the differences in diagnostic methods and criteria.

Over the past 20 years, uniformisation of diagnostic criteria has allowed across country comparison [15-18]. Epidemiological studies carried out in the 90's also provided the evidence of the rising prevalence of diabetes all over Africa. The global estimates of the number of people with diabetes in Africa was approximately 3 millions in 1994 and was due to go through a 2-3 fold increase by the year 2010 [19].

The highest prevalence is found in adult populations of Indian origin, followed by Black populations and Caucasians [20-21]. Among the population of Indian origin of South Africa and Tanzania, the prevalence is between 12 and 13%, but is lower than that of American Indians [21-23]. The prevalence in Blacks follows a westernisation gradient, with that of rural Africa found below 1%, and urban Africa between 1 and 6%. The black populations of the Caribbean have a 10-13% prevalence, and African-Americans between 12 and 15% or higher [2, 24-41]. The prevalence of diabetes in Caucasians of Africa is comparable or higher than their European counterpart, between 6 and 10% [42, 43].

The majority of the patients (70-90%) present with typical Type 2 diabetes, and up to 25% of patients with diabetes mellitus are diagnosed with Type 1 diabetes [3, 44]. Variable proportions present with tropical diabetes (~ 1%), or with ketosis-prone atypical diabetes (~ 10-16%). The incidence of type 1 diabetes mellitus varies from 4 to 10/100.000 among the 0-19 yr old population in Africa [45-47]. In African-Americans, the incidence is 11/100.000/yr [48]. A recent study in Philadelphia found a 14.3/100.000/yr incidence of Type 1 diabetes in African American children aged 0-14 yr and 25.3/100.000/yr in the 10-14 yr age group, raising the question of potential misclassification of these patients [49], as Type 2 diabetes is known to be increasing in children of African origin [50].

Risk factors

The identified risk factors are not markedly different from those reported in other populations. They can be classified as non-modifiable and modifiable risk factors.

Age and ethnicity are the main non-modifiable determinants of diabetes prevalence in Africa as confirmed by the increasing prevalence with age, and the difference between Indian, Black and Caucasians in South Africa. Indians have the highest predisposition and are followed by Blacks and Caucasians.

Among the modifiable risk factors, residence seems a major determinant, since urban residents have a 1.5 to 4-fold higher prevalence of diabetes compared to their rural counterpart [51]. This is attributable to lifestyle changes associated with urbanisation and westernisation.

Urban lifestyle in Africa is characterised by changes in dietary habits involving an increase in consumption of refined sugars and saturated fat, and a reduction in fibre intake [52, 53]. Moreover, there is a

reduction in physical activity associated with urban lifestyle. Rural populations rely upon foot walk as transportation means and often have intense agricultural activities as their main occupation [54]. Rural dwellers therefore have a high physical activity related energy expenditure compared to urban subjects [55, 56], thus explaining the higher rates of obesity in the cities. Obesity is also at least 4 times higher in urban areas compared to rural [57].

The population of Africa is predominantly rural (34% urban); however, the 1995-2000 urban growth rate was estimated at 4.3% (compared to 0.5% in Europe) [58]. Thus, more than 70% of the population of Africa will be urban residents in 2025 [58]. A tremendous increase in the prevalence of diabetes attributable to rapid urbanisation is therefore expected. Moreover, life expectancy at birth was also rapidly increasing. For example, in 1960 it was around 35 years in Cameroon and rose to approximately 55 years in 1990. An increment in the prevalence due to the change in the age structure of the population is also expected. It is therefore understandable why by the year 2025 the majority of the world diabetes population will be living in the developing countries. In fact, it is estimated that while there will be a 42% increase of diabetes prevalence in the developed countries, the developing countries will go through a 170% increase between 1995 and 2025 [7]. Thus, by the year 2025, over 75% of people with diabetes will reside in developing countries [7]. These estimates and projections should however be modulated by taking into consideration the ongoing HIV infection pandemics.

The higher prevalence of Type 2 diabetes in a given environment in Africans compared to Caucasians, suggests a genetic predisposition. To the best of our knowledge, no large-scale genome scan analysis has been reported, nor mutations of candidate genes described. It has been reported that 19% of diabetic patients in a Dakar (Senegal) hospital had a missense mutation Gly574Ser in the transcription factor HNF-1alpha, however the same mutation was found in 33% of the control population [59]. The ongoing Africa America Diabetes Mellitus (AADM) study that aims to map type 2 diabetes mellitus susceptibility genes in West Africans and African-Americans will probably enable a better insight of this question [60].

The HLA alleles and haplotypes of susceptibility of Type 1 diabetes are the same as those reported in other populations. There are however some regional specificities. DR4 alleles are infrequent in Central Africa, and DR9 allele has been reported to be associated with Type 1 diabetes in Senegal and South African Zulus [61-65].

■ CLINICAL SPECIFICITIES

Diabetes is characterised in Africans, by a high rate of acute and long-term complications and the existence of atypical presentations. Several authors have also pointed out the difficulty in classifying a non-negligible proportion of patients, due to the atypical presentation and clinical course [4, 44, 66]. They include patients with tropical diabetes mellitus that represents less than 1% of the cases and might be related to malnutrition; and an atypical diabetes presenting as type 1 diabetes at onset, with a subsequent clinical course of type 2 diabetes, or prolonged remission. This form of phasic insulin dependent diabetes has been described in reports from Africa in the 60's and 70's, and was mostly characterised in the US in children and young adults of African ancestry, and classified as idiopathic Type 1 diabetes, or Type 1b [67-69]. We discuss this clinical entity in the second part of the review.

Tropical diabetes

The first reference to this subtype was published in 1907 [70], but it is Hugh-Jones who provided the first description of what he named J-type diabetes in 13 patients from Jamaica [71]. Several subsequent descriptions of a similar presentation with various names were provided from Indonesia, Uganda, India and several other countries, with various names [72-75].

The 1980 WHO technical report on diabetes recognised tropical diabetes as a specific type. Two main types were recognised, the protein deficiency pancreatic disease and the fibrocalculous pancreatic disease [15]. The main characteristics of this type of diabetes were: severe hyperglycaemia, onset before the age of 30, body mass index under 18 or 19 kg/m^2, absence of ketosis when insulin is withdrawn, high daily needs in insulin ($\geq$ 1.5UI/kg/j), poor socio economic status or history of childhood malnutrition, inconstant abdominal pains, pancreatic calcifications in the absence of heavy alcohol intake, hyperparathyroidism or gallstones (Fibrocalculous pancreatic disease) [76].

Malnutrition was incriminated as an etiological factor, and the disease was called malnutrition related diabetes mellitus. However, evidence was still sparse on the pathogenesis. In fact over the course of kwashiorkor, a state of severe protein and energy deficiency, there is a tendency to the reduction of insulin secretion and impaired glucose tolerance which seems however reversible [77]. Moreover, it is uncertain whether the signs of malnutrition may have developed as a consequence of longstanding uncontrolled diabetes with poor nutritional intake or if diabetes developed secondarily to malnutrition. The prevalence of malnutrition related diabetes mellitus is not increased in areas of the world where malnutrition is high [77].

McMillan *et al.* observed that tropical diabetes areas coincided with parts of the world where cassava (Manihot esculenta) served as staple food and the hypothesis that cyanogenic glycosides (linamarin and lotusaustralin) may cause damage to pancreatic islet cells was drawn [78]. In malnutrition, cyanide may

not be detoxified and therefore cause damage to the pancreas and the thyroid gland. Experimental evidence to support this hypothesis is weak [77]. In animal models, long term cassava feeding does not cause diabetes [79]. Swai *et al.* compared two rural populations in Tanzania of which one had cassava as staple food and raised plasma and urinary cyanides, and did not observed any difference in the glucose tolerance or the prevalence of diabetes in both settings [80]. Thus, there is no strong evidence from available literature to support the hypothesis that cassava consumption may cause tropical diabetes.

Acute complications

Infection is the revealing mode of diabetes in 22% of the patients [81]. In Burkina Faso, over a 6-yr follow-up period, 79% of a cohort of diabetic patients had had at least one episode of infection [82].

In difficult socio economic situations, there is a high rate of metabolic complications and type 1 diabetes is associated with high rates and early mortality. Gill *et al.* reported 16% mortality in 64 type 1 diabetic patients over a 10-year follow up period, one half due to sepsis and keto-acidosis [83]. Among 144 patients admitted over a 6 yr period for acute complications in a hospital in Nigeria, 25 patients deceased, including 2 who could not afford insulin treatment [84].

Long term complications

Greater prevalence of diabetes complications has been reported in populations of African origin compared to Caucasians [85, 86]. Genetic predisposition has been suggested as a possible explanation but has never been confirmed. High blood pressure and impaired metabolic control are among the main determinants of the progression of diabetes vascular complications [87]. The prevalence of hypertension is high in population of African ancestry [38] and is frequently inappropriately controlled [88]. Similarly, inadequate blood glucose control is frequently reported, due to poor compliance and/or difficult access to appropriate care, and affordability of treatment in difficult socio-economic environment [89-91]. Although genetic predisposition may not be ruled out, blood pressure and blood glucose control are major confounders; therefore the increased prevalence in microvascular complications is difficult to interpret.

Retinopathy

Africans seem more at risk than Indians and Caucasians, since in a multiethnic cohort of comparable known duration of diabetes, they had the highest prevalence of retinopathy [92]. The overall reported prevalence of diabetic retinopathy varies between 15 and 55% in Africa [92-97]. Late diagnosis of diabetes is frequent, thus, at diagnosis, up to 21 - 25% of type 2 patients and 9.5% of type 1 may already present with retinopathy [92, 98, 99]. Macular oedema or ischaemia and/or proliferative retinopathy are present in 15% of the patients with retinopathy [94, 100].

Nephropathy

Incipient nephropathy is reported in 32 to 57% of patients with mean known duration of diabetes of 5 - 10 years in some hospital-based studies [92, 100, 101]. Overt proteinuria is reported in 5.3 to 28% of the patients, and increases with diabetes duration [93, 94], and one third of the patients admitted to most dialysis units in Africa have diabetes [102]. In a South African cohort, one half of the mortality of type 1 diabetic patients was reported in patients in renal failure [83]. Unrecognised parasitic and sickle cell proteinuria must however be taken into consideration when interpreting these data.

Neuropathy

The frequency of symptoms of peripheral neuropathy varies from 9.5 to 36.4%, and erectile dysfunction has been reported in up to 49% of diabetic patients [93, 103-105]. Cardiac autonomic neuropathy was reported in 32% of a 50-patient type 1 diabetic population [106]. Neuropathy also occurs early in the course of the disease, but seems less influenced by the duration of diabetes than retinopathy and nephropathy. Poor blood glucose control is significantly associated with this complication [107]. Ethnic differences may exist, since population from Maghreb are found to experience severe neuropathy more often than other ethnic groups [108].

Cerebrovascular disease

Due to the mortality associated with cerebrovascular disease, and therefore the low proportion of patients seen at the hospital, its incidence is difficult to evaluate. However, it is known that due to the high prevalence of untreated hypertension, stroke mortality is high in Africa, 3 to 6-fold that of England and Wales [109].

Coronary artery disease

Macrovascular complications of diabetes are lower in Africa compared to the western world. However, cardiovascular morbi-mortality is higher in Africans living in developed countries. In Africa, the prevalence of electrical ischaemia (EKG effort testing) is between 5.1 and 8.7% in diabetic patients [93, 110]. This might be underestimated due to the scarcity of diagnostic facilities (coronarography and myocardial scintigraphy).

Left ventricular hypertrophy and dysfunction has been demonstrated in African diabetic patients and

may account for the excess of congestive heart failure. Up to 50% of asymptomatic patients may present with these abnormalities [110, 111], however appropriate comparison of ventricular indexes with matched background population is still lacking.

Lower limb arteriopathy and diabetic foot

Depending on the diagnostic criteria (absence of pulse on clinical examination or Doppler evidence of vascular lesion), the prevalence of peripheral vascular disease varies from 4.4% to 28% [112, 113].

Lower extremity amputation in diabetic patients varies from 1.4% to 6.7%, and active foot ulceration may concern up to 11.9% of hospital diabetic populations [114]. The mean age at amputation was 37 yr in type 1 and 59 yr in type 2 diabetic patients out of a 2250-patient cohort, with 20% due to ischaemic gangrene [115]. In fact, arteriopathy seems to contribute to a lesser extend than neuropathy and infection to the development of diabetic foot lesions in Africans [114].

In summary, it is believed that macrovascular complications of diabetes occur less often in patients in Africa compared to Africans living in developed countries and Caucasians. By contrast, there is an excess in microvascular complications in population of African origin both in Africa and in developed countries which raises the question of a possible predisposition. However, high prevalence of uncontrolled hypertension and poor metabolic control are confounders.

■ CONCLUSION

The prevalence of diabetes mellitus in population of African origin is on the rise due to urbanisation, westernisation and their associated lifestyle changes, increasing life expectancy at birth and possibly a genetic predisposition. In fact there is a clear rural - urban positive gradient in the prevalence of diabetes and its risk factors. Thus, diabetes will represent a heavy burden on health systems in the years to come, mainly due to its high prevalence, and its acute and long-term complications. The design and implementation of a strategy for early diagnosis and appropriate population-based prevention programme is therefore a public health and economic priority.

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