The variable African diabetic phenotype: tales from the north and the south

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Abstract

Although most African diabetic patients are clearly phenotypically type 1 or 2, some do not easily fit into these categories. Examples are malnutrition-related diabetes mellitus (MRDM) and atypical ketosis-prone type 2 diabetes. To explore this problem we have compared two cohorts of diabetic patients from very different parts of Africa – rural KwazuluNatal in South Africa, and Mekelle District in northern Ethiopia. Basic demographic data were collected as well as measurements of blood pressure (BP) and glycated haemoglobin (HbA_{1c}). South African patients were older (56±11 vs 41±16 years, p<0.001) than Ethiopian patients, and more were female (70% vs 30%, p< 0.001). Body mass index (BMI) was higher in South African patients (31.5±6.3 v 20.6±5.4, p<0.001) and 56% were obese (BMI >30.0) compared with 4% in Ethiopia (p<0.001). Hypertension (BP >140/80) affected 80% of South African patients but only 4% of the Ethiopian cohort (p<0.001). Insulin treatment was more common in the Ethiopian patients compared with South Africans (66% vs 25%, p<0.001). Duration of diabetes and HbA_{1c} were similar in both groups. Phenotypically, 96% of the South Africans had typical type 2 diabetes, whereas only 42% of the Ethiopians had such type 2 characteristics (p<0.001). The high occurrence of apparent type 1 diabetes (42%) in the Ethiopian patients, in conjunction with their very low BMI levels and local chronic food shortages, raises the possibility as to whether at least some of this group may have MRDM.

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Introduction

The globally increasing problem of diabetes is well known, and in Africa the prevalence is increasing more rapidly than in developed countries. This is placing a major burden on poorly resourced healthcare systems, which are already struggling to cope with the problems of HIV/AIDS, tuberculosis, and malaria.[1]

Throughout the world, most diabetic patients can be readily classified as type 1 or type 2. The same is mainly true in Africa, but in certain parts of the continent, difficulties of classification occur. This paper explores the variability and heterogeneity of the diabetic phenotype in Africa, using as examples two populations of diabetic patients from the north and the south of the continent.

The diabetes phenotype – north and south

Hlabisa District is a remote area of northern KwazuluNatal, in the south-eastern part of South Africa. It has a central hospital with several peripheral primary healthcare clinics. The area is rural, although there are two relatively close towns. As part of a long-term project exploring optimal ways of delivering diabetes care in the district, a group of 320 diabetic patients were enrolled.[2,3] Their baseline demographic and control features are shown in Table 1.

From the far south of the continent, we move to the far north. Mekelle District is in northern Ethiopia, close to the Eritrean border. The town of Mekelle is at the centre of the region, with a moderate-sized district hospital. Surrounding the town are large rural and arid areas populated by subsistence farmers. In Mekelle, a study of 105 consecutively attending patients at the hospital diabetic clinic by chance recorded the same demographic and control data as in the Hlabisa study.[4]

Methods of comparison

The patient populations and methods of data collection have been previously described in both Hlabisa (South Africa)[3] and Mekelle, Ethiopia.[4] Demographic data were collected in the same way on both sites. Obesity was defined as a body mass index (BMI) of >30.0 kg/m^2, and hypertension as a resting blood pressure (BP) by mercury sphygmomanometer of >140/80. Glycated haemoglobin (HbA_{1c}) was measured by boronate affinity chromatography in Mekelle, and high performance liquid chromatography (HPLC) in Hlabisa, but both methods were DCCT-aligned,[5] and therefore, directly comparable.

The Ethiopian patients attended a central hospital diabetic clinic, whereas most of the South African patients attended peripheral primary healthcare clinics. However, many of the Ethiopian patients came from outside Mekelle, as there is little diabetes care available at peripheral clinics in this location.

Statistical analysis was carried out using a statistical package. Data were compared by Student's unpaired t test, or for proportionate data Fisher's exact test.

Results

Information from the two surveys, with statistical significance, is shown in Table 1. The differences are striking. Though both groups had a similar mean duration of diabetes (7 years), the Ethiopian patients were significantly younger (41±16 v 56±11 years, p<0.001), and there was a reversal of gender ratio (30% male in Hlabisa and 70% male in Mekelle, p<0.001). Defining type 1 diabetes as an onset below 30 years of age and the need for insulin from diagnosis, 4% of the South African group had type 1 disease, compared with 42% in Ethiopia (p<0.001). BMI was strikingly different (31.5±6.3 in South Africa vs 20.6±5.4 in Ethiopia, p<0.001). Some 56% of the South African group were obese, but only 4% of the Ethiopians (p<0.001). BP measurement showed 80% in Hlabisa to have hypertension, compared with only 5% in Mekelle (p<0.001). Most patients in Hlabisa were on treatment with oral agents (71%), but insulin was the commonest therapy in Mekelle (66%) – p<0.001.

Sadly one similarity between the two groups was very poor glycaemic control: HbA_{1c} was 11.1±4.2% (Hlabisa) and 11.3±2.8% (Mekelle) – as expected not significantly different.

Table 1 Comparison between rural diabetic patients from South Africa (Hlabisa) and Ethiopia (Mekelle)

	South Africa (Hlabisa)	Ethiopia (Mekelle)	Significance
Number	320	105	
Age (years)	56±11	41±16	p<0.001
Sex (M:F)	96:224 (30%:70%)	74:31 (70%:30%)	p<0.001
Duration DM (years)	7±6	7±6	pNS
DM type (1:2)	12:308 (4%:96%)	44:61 (42%:58%)	p<0.001
BMI (kg/m^2)	31.5±6.3	20.6±5.4	p<0.001
Obese (BMI >30.0)	179 (56%)	4 (4%)	p<0.001
Treatment	Diet 13 (4%) OHA 227 (71%) Insulin 80 (25%)	Diet 1 (1%) OHA 35 (33%) Insulin 69 (66%)	pNS p<0.001 p<0.001
Systolic BP (mmHg)	141±26	108±17	p<0.001
Diastolic BP (mmHg)	87±5	72±11	p<0.001
Hypertension (>140/80)	256 (80%)	5 (5%)	p<0.001
HbA_{1c}	11.1±4.2	11.3±2.8	pNS

Note: Type 1 is defined as onset of diabetes <30 years of age and on insulin from diagnosis.
BP = blood pressure,
BMI = body mass index,
DM = diabetes mellitus,
OHA = oral hypoglycaemic agents.

Is 'type 1' always type 1?

The Hlabisa patients (South Africa) are mostly classical type 2 patients – overweight or obese, middle-aged, frequently hypertensive, and mostly on oral agent treatment. The predominance of female patients (70%) may represent health-seeking behaviour and/or migratory patterns of male patients working in nearby towns.

But what of the Mekelle (Ethiopian) patients? They were younger, much thinner (mean BMI 20.6), mostly male (70%), rarely hypertensive, and frequently on insulin treatment (66%). By standard definitions, a remarkable 42% have type 1 disease. Type 1 diabetes is generally regarded as rare in Africa,[6] and survival is poor.[7] Interestingly, black African type 1 patients tend to present with their disease a decade later than white type 1 counterparts (median 23 years versus 12 years).[8]

If type 1 diabetes is rare and frequently fatal in Africa, why are so many young, thin diabetic patients on insulin treatment seen in northern Ethiopia? The apparently high occurrence of type 1 diabetes in this area has been recorded previously by other observers[9] – Watkins, for example, called the type 1 prevalence in Gondar (northern Ethiopia) 'astonishing'.[10] A more recent and detailed study from the same area has had similar findings.[11] One answer may be that this is an area of persisting drought and famine, and the suggestion has been made that the patients may have 'malnutrition-related diabetes mellitus' (MRDM) rather than true type 1 disease.[9,11]

Malnutrition and diabetes?

The concept of past or present malnutrition being a causative factor in the development of diabetes, is an old and contentious one.[12] Patients with MRDM are underweight, predominantly male (a male to female ratio of approximately 2:1), young, and hyperglycaemic, but ketosis-resistant. They almost all are treated with insulin (and thus may resemble type 1 diabetic patients) but do not develop ketoacidosis on insulin cessation.[12,13] In some cases, there is clear pancreatic disease with

steatorrhoea and radiological calcification – the syndrome of 'FCPD' (fibrocalculous pancreatic diabetes). In other instances, there is a typical clinical picture of MRDM, but no evidence of exocrine pancreatic disease. This is known as 'MMDM' or malnutrition-modulated diabetes mellitus.[1]

The concept of MRDM has come in and out of favour over the last three decades, but interest has returned recently, particularly related to descriptions from northern Ethiopia.[9,11] From Table 1, it can be seen the large numbers of patients from the Mekelle area of Ethiopia with apparent type 1 diabetes, could have MRDM. They are young, thin, insulin-treated, and have a male predominance. The long-standing presence of food shortage and famine in northern Ethiopia would also support the presence of MRDM in this area.

'Atypical' diabetes in Africa

To further complicate matters, an 'atypical' form of diabetes has been described, largely from West Africa. Such patients are variably insulin-requiring, usually lack islet antibodies, but can be ketosis-prone. The condition has been described as 'ketosis-prone atypical type 2 diabetes mellitus',[14] and appears to also occur in Afro-Americans in the USA where it is sometimes called 'flatbush diabetes'.[15] Like MRDM, there is a male excess, and the presentation is at a young age and often clinically abrupt, with extreme hyperglycaemia and/or ketoacidosis; though later patients often 'remit' and are easily controllable on oral agents. An interesting finding in 'atypical' African diabetes is that it has been recently reported that the majority of patients demonstrate antibodies to herpesvirus 8 (HHV-8).[16] Perhaps the disease is caused by an acute viral 'insulitis', with later partial or complete remission.

Conclusions

Using the examples of clinical surveys on diabetic populations in the north (Mekelle, Ethiopia) and south (Hlabisa, South Africa) of the African continent, this paper has demonstrated how the African diabetic phenotype can be far more variable than elsewhere in the world. 'The syndromes of MRDM and 'atypical type 2 diabetes' are increasingly being recognised and accepted. At least in certain parts of Africa, the simple division of the diabetic syndrome into type 1 or type 2 may be too simplistic a classification.

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