Research from the South

Macrovascular disease in diabetics in Central Africa

M ROLFE

Abstract

Six hundred African diabetics were examined for evidence of large vessel disease using a standardised technique based on the World Health Organisation Multinational Study, in which no country from Africa was represented. Twelve patients had electrocardiograms coded coronary probable using Minnesota coding. Seven patients had had strokes and 10 peripheral vascular disease. Despite the high prevalence of hypertension large vessel disease was uncommon, being comparable with Japan and Hong Kong, who had the lowest prevalence in the WHO study. Overall, only 49 patients had evidence of macrovascular disease.

Introduction

Historically, the prevalence of large vessel disease in Africans with diabetes has been low (table I) despite the high prevalence of hypertension. Myocardial infarction and peripheral vascular disease are rare, and most cases of gangrene are due to a combination of neuropathy and infection. In 1979 the World Health Organisation (WHO) reported on a multinational study of diabetes whose object was to compare the prevalence of microvascular and macrovascular disease in different populations using a standardised questionnaire and examination technique.[1] Fourteen centres in 13 countries throughout the world participated, but unfortunately no country from Africa was represented. There are wide discrepancies in the reported prevalence of the various complications of diabetes in Africans owing to the diversity of methods and criteria used and failure to take the patient's age and duration of diabetes into account.

This paper reports a study of large vessel disease in Africans with diabetes that was part of a detailed assessment of diabetes and its complications in Central Africa. A standardised technique based on the WHO protocol was used thus giving a more accurate estimate of the prevalence of large vessel disease and allowing comparisons to be made with other countries.

TABLE I—*Reported prevalence of large vessel disease in Africans with diabetes*

Disease and country	Year and reference	Prevalence %
Heart:		
Ethiopia	1984[2]	1
Kenya	1972[3]	15·6
Nigeria	1968[4]	1
	1971[5]	1
South Africa	1966[6]	6, 8
	1970[7]	17
	1977[8]	10
Tanzania	1980[9]	23
Uganda	1962[10]	2·6
Stroke:		
Ethiopia	1984[2]	1·3
Nigeria	1968[4]	1
	1971[5]	6
Tanzania	1980[9]	1·4
Peripheral vascular disease:		
Ethiopia	1984[2]	0·6
Nigeria	1968[4]	0
	1971[5]	0·2
South Africa	1984[11]	2
Zimbabwe	1963[12]	0

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Methods

PATIENTS

Six hundred ethnic Africans (372 men, 228 women) were recruited into the study who were being treated for diabetes in general medical clinics at seven hospitals belonging to Zambia Consolidated Copper Mines Ltd and at two government hospitals, all situated in the copperbelt region of Zambia. The hospitals did not keep registers of diabetic patients, but patients attended hospital rather than private practitioners to receive free medicine. Physicians were asked to compile lists of patients with diabetes some three months before the study.

I saw and examined about 90% of the diabetics who attended each hospital, though this is an estimate. Nearly all the men and over half of the women spoke English. A control group was also examined to compare the prevalence of hypertension and abnormal electrocardiographic findings in the general population. As this was likely to be extremely low in young Africans, only people aged 35 or over were selected. They were matched by age and sex with the diabetic patients. As some patients (diabetic and control) were uncertain of their age, they were matched in five year age groups: 35-39, 40-44, and so on, each group containing the same number of diabetic patients and control patients.

The 469 control patients (297 men, 172 women) were selected from three sources. Patients who were known to have diabetes were asked to bring two friends or relatives of similar age. Because insufficient numbers were recruited (40; 8·5%) patients who were on the surgical wards for minor operations were taken at random (115; 24·5%). The third group were patients attending a mission hospital in a rural area 30 km from Kitwe, which serves a population of about 7000 people. They were selected by the sisters who ran a general outpatient clinic on the basis of age and the patient's willingness to be examined (314; 67%). Nearly all of those who were asked to act as controls responded positively. All control patients were asked if they were known diabetics (none), and all had a urine sample tested for glucose. Only those whose urine samples were negative were admitted to the control group (all).

COLLECTING DATA

A questionnaire was completed for each patient. For those who did not understand English a Zambian nurse translated from a prepared sheet in the local dialect, Bemba. The name, sex, date, tribal origin, age, and age at diagnosis of diabetes were recorded. The exact age was not always known, especially by older women, and occasionally had to be estimated from the patient's physical appearance, after consulting with the attending Zambian nurse. This estimation was helped by asking the date of the last menstrual period, the menopause being taken to be at 50 years of age. Age had to be estimated for about eight (2%) men and 60 (26%) women in the study group. The duration of diabetes was calculated from the age at diagnosis and by information given by the patient and from hospital records. Details of current treatment were recorded. Cigarette smoking was classified as present, past, or absent.

The patients were then asked the following questions based on the WHO questionnaire but adapted for an African population: (1) Have you ever had severe pain across the front of your chest lasting more than 30 minutes? (2) Do you get pain or discomfort in the chest when walking or running? (3) If yes, is it relieved by resting? (4) Do you feel the pain anywhere else? (5) Do you get the pain in your legs when walking? If yes, indicate where. (6) Is it relieved by resting? (7) Has the patient ever suffered from ischaemic gangrene or had amputation of toe, foot, or leg for arterial disease? (8) Have you ever had weakness or loss of strength of arm or leg lasting more than one day? A positive response to question 1 was taken to indicate possible myocardial infarction; questions 2-4 related to angina pectoris; questions 5-7 to peripheral vascular disease; and question 8 to the presence of cerebrovascular disease.

A physical examination was then undertaken. The blood pressure was measured immediately the questionnaire had been completed. A mercury sphygmomanometer was used with a cuff measuring 23×14 cm (bladder 23×13 cm). The pressure was measured in the right arm with the patient sitting. The systolic pressure was recorded as the first perception of successive sounds. The diastolic fourth phase was recorded at which sounds became muffled and the fifth phase at which sounds disappeared. All readings were recorded in mm Hg to the nearest 2 mm, reading the calibration below the meniscus. Patients were defined as hypertensive if they had a systolic pressure ⩾160 mm Hg or a diastolic pressure ⩾95 mm Hg recorded at the fifth phase, or both, or were under treatment with hypotensive drugs. If the fifth phase was not audible the fourth phase muffle was taken. The height of each patient without shoes was recorded in cm and the weight without coat or shoes recorded in kg. The body mass index (BMI) was calculated according to the formula BMI=weight in kg divided by the height in m^2.

A 12 lead resting electrocardiogram was recorded with the patient supine and fasting. Initially this was performed on all patients, but later patients under 20 years of age were excluded. The results were subjected to Minnesota coding[13] in London by the same two observers who had coded for the WHO Multinational Study. The results were grouped into three categories: coronary probable included all those coded 1-1 and 1-2 (large Q and QS waves) and 7-1 (complete left bundle branch block); coronary possible included those coded 1-3 (small Q waves), 4-1, 4-2, 4-3 (S-T segment abnormalities), and 5-1, 5-2, and 5-3 (T wave abnormalities). All other codings were regarded as normal. A resting 12 lead electrocardiogram was recorded on control subjects, and blood pressure was measured as previously described.

Lipoprotein analysis was performed in the department of chemical pathology at the University of Witwatersrand, Johannesburg, South Africa. Serum was separated as soon as possible after collection and frozen at −20°C. Samples were transported to Johannesburg frozen, and all estimations were completed within one week after they were received to guard against changes in the lipoprotein fractions with prolonged storage. Cholesterol and triglyceride concentrations were determined enzymatically using Boehringer-Mannheim kits (catalogue numbers 692905 and 701882 respectively). High density lipoprotein cholesterol was measured after precipitation of low density lipoprotein and very low density lipoprotein with phosphotungstate and magnesium chloride.[14] Calibration and control materials for measuring cholesterol and triglyceride concentrations were obtained from the Clinical Chemistry Standardization Section, Centers for Disease Control, Atlanta, USA. A control sample for all estimations was inserted after every twelfth specimen. The coefficient of variation for cholesterol, triglycerides, and high density lipoprotein cholesterol was <2%, <4%, and <5% respectively at both low and high levels.

All results were entered on to an IBM personal computer employing Lotus 1-2-3 database software. Statistical analysis was done using Student's *t* test or the χ^2 test.[15]

Age adjustment for the major variables was performed by computer analysis using the package Generalised Linear Interactive Modelling.[16] Analysis of covariance was performed and tested if an assumption of parallelism was valid. If the test showed that it was unreasonable to assume parallelism—that is, significant result at 5% level—then the mean for the respective variable was reported unadjusted for age since adjustment would not have been meaningful. Comparisons were reported with nominal levels of statistical significance at the 5% and 1% levels. These should be interpreted with caution where multiple comparisons were made.

Results

Six hundred Africans with diabetes were examined (372 men and 228 women).

HEART DISEASE

Diabetics

Of the 589 patients who had electrocardiograms, analysis of the Minnesota coding results showed that 12 (2%) were coded coronary probable and 91 (15%) coronary possible. The proportion of men and women in each group was approximately equal (table II). In men there was no difference in age or duration of diabetes between those coded normal (disease free) and those coded coronary possible. Men who were coded coronary probable were older than those coded coronary possible (mean 14·4, 95% confidence intervals 5·0 to 23·8; t=3·06, df=60, p<0·01) and those who were disease free (mean 17·7, 95% CI 8·4 to 27·0; t=3·73, df=315, p<0·001).

Women coded coronary possible were older than those who were disease free (mean 9·9, 95% CI 5·3 to 14·5; t=4·23, df=221, p<0·001). After adjustment for age duration of diabetes was statistically significantly longer in men coded coronary probable (table II), but there was no difference in women. Systolic blood pressure was statistically significantly higher in men coded coronary possible than in those who were disease free. There was no difference in mean body mass index or mean total cholesterol or triglyceride concentrations between the three groups for either sex, but women who were coded coronary possible had a higher high density lipoprotein cholesterol than those who were disease free.

Symptoms of heart disease were commoner in women (p<0·05 for possible infarction, p<0·02 for angina): 28 (12%) women had angina and 10 (4%) possible infarction, while the corresponding figures for men were 25 (7%) and six (2%). Three out of 10 women gave affirmative answers to both possible infarction and angina, compared with five out of six men. Comparison with the Minnesota coding results showed that six of the 28

TABLE II—*Mean duration of diabetes, blood pressure readings, body mass index (BMI) and lipid concentrations according to Minnesota coding for 372 men and 228 women adjusted for age*

	Normal		Coronary possible		Coronary probable	
	Men	Women	Men	Women	Men	Women
No (%)	310 (83)	187 (82)	55 (14·8)	36 (16)	7 (2)	5 (2)
Mean (SD) age (years)	45·0 (12·5)	42·4 (13)	48·3 (12)	52·3 (13·5)	62·7 (5·5)	49·2 (12)
Range	9-72	12-71	21-72	18-80	55-70	28-65
No (%) hypertensive	99 (32)	73 (39)	32 (58·2)	24 (66·7)	4 (57)	3 (60)
Duration of diabetes (years)	1·1	2·1	1·3	2·5	6·4*†	1·7
Systolic blood pressure (mm Hg)	96·9	93·2	108·8**	94·2	106·4	109·6
Diastolic blood pressure (mm Hg)	67·8	65·5	71·3	65·6	63·6	68·2
BMI	19·6	21·6	20·4	20·3	18·9	19·4
Total cholesterol (mmol/l)	3·77	3·60	3·89	3·74	3·65	4·33
High density lipoprotein cholesterol (mmol/l)	1·01	0·90	1·08	1·03*	1·03	0·94
Triglyceride	1·57	1·50	1·65	1·18	1·46	1·18

*Significantly different from normal group at 5% level (** at 1% level)
†Significantly different from coronary possible group at 5% level.

women had an abnormal electrocardiogram (five coronary possible, one coronary probable) and 11 of 25 men (10 coronary possible, one coronary probable). Two of the six men with symptoms of possible infarction had abnormal electrocardiograms (one coronary possible, one coronary probable) compared with five of the 10 women (four coronary possible, one coronary probable).

Control subjects

Forty five (10%) of the control group were coded coronary possible, comprising 27 women and 18 men. The men were significantly older (mean 5·7, 95% CI 0·6 to 10·8; t=2·26, df=43, p<0·05). Hypertension was more prevalent (p>0·05) in women but the mean systolic and diastolic pressures were not significantly different. One control subject was coded coronary probable, a man aged about 62, who was normotensive. Comparing control subjects who were matched for sex and age with the diabetics (table III) showed that the prevalence of Minnesota coding coronary possible was higher in men diabetics than controls (p<0·001), but there was no significant difference between women diabetics and controls.

TABLE III—*Mean age and blood pressure (mm Hg) in control and diabetic patients (aged 35 and over) coded coronary possible*

	Controls	Diabetics
	Men	
No (%)	18 (6·1)	48 (16·2)
Mean (SD) age (years)	56·2 (6·2)	52·0 (7·8)
No (%) hypertensive	3 (16·7)	32 (66·7)
Mean (SD) systolic pressure	139·9 (30·6)	156·8 (31·0)
Mean (SD) diastolic pressure	81·2 (15·6)	89·6 (15·4)
	Women	
No (%)	27 (15·7)	32 (18·6)
Mean (SD) age (years)	50·5 (9·4)	55·8 (10·1)
No (%) hypertensive	7 (26)	23 (72)
Mean (SD) systolic pressure	132·4 (22·6)	151·5 (24·2)
Mean (SD) diastolic pressure	75·9 (13·9)	85·9 (13·7)

There was no difference in age between the diabetics and control subjects coded coronary possible, but hypertension was far more prevalent (p<0·001) in the diabetics. Although the mean systolic pressure was higher in the diabetics, this was significant only in women (mean 19·1, 95% CI 6·8 to 31·4; t=3·11, df=57, p<0·01).

CEREBROVASCULAR DISEASE

Strokes were documented in seven patients, five men and two women. All had been admitted to hospital, and five showed evidence of residual disability. They were older (mean 14·5, 95% CI 4·5 to 24·5; t=2·84, df=598, p<0·01) than patients without cerebrovascular disease. After adjustment for age duration of diabetes was statistically significantly shorter in patients with cerebrovascular disease than in those without, but other variables showed no difference between the two groups (table IV). Six patients, however, were taking hypotensive drugs.

TABLE IV—*Comparison of mean duration of diabetes, blood pressure readings, body mass index (BMI), and lipid concentrations in patients with and without cerebrovascular disease adjusted for age*

	A: cerebrovascular disease	B: No disease	SE (B−A)*	*t* value
No (%)	7 (1·2%)	593 (98·8)	—	—
Mean (SD) age	59·0 (5·8)	44·5 (13·5)	—	—
No (%) hypertensive	6 (85·7)	229 (38·6)		
Duration of diabetes (years)	−3·3	1·0	1·90	2·25†
Systolic blood pressure (mm Hg)	92·6	94·3	9·66	0·18
Diastolic blood pressure (mm Hg)	63·3	65·8	2·43	1·00
BMI	19·4	20·2	1·85	0·46
Total cholesterol (mmol/l)	4·23	3·72	0·46	−1·10
High density lipoprotein cholesterol (mmol/l)	1·09	0·96	0·17	−0·14
Triglyceride (mmol/l)	1·51	1·53	0·40	0·05

*Standard error of mean difference between B and A.
†Significant at 5% level.

PERIPHERAL VASCULAR DISEASE

Three women and six men had intermittent claudication. Two men had had amputations for peripheral vascular disease, one of whom also gave a history of claudication in the other leg. All the women had normal electrocardiograms, but six of the seven men were coded coronary possible. Two of the latter also gave a history of angina. After age adjustment (table V) systolic blood pressure was statistically significantly higher in patients with peripheral vascular disease compared with those without, but there was no difference in the other variables.

TABLE V—*Comparison of mean duration of diabetes, blood pressure readings, body mass index (BMI), and lipid concentrations in patients with and without peripheral vascular disease adjusted for age*

	A: with disease	B: no disease	SE (B-A)*	*t* value
No (%)	10 (1·7)	590 (98·3)	—	—
Mean (SD) age (years)	46·5 (7·1)	44·7 (13·6)	—	—
No (%) hypertensive	6 (60)	229 (38·8)	—	—
Duration of diabetes (years)	3·5	1·1	1·59	−1·52
Systolic blood pressure (mm Hg)	116·1	94·1	7·99	−2·76**
Diastolic blood pressure (mm Hg)†	88·0	81·5	5·06	−1·28
BMI	19·5	20·3	1·54	0·50
Total cholesterol (mmol/l)	3·62	3·70	0·36	0·23
High density lipoproteins (mmol/l)	0·94	0·96	0·02	0·16
Triglycerides (mmol/l)	1·59	1·53	0·31	−0·20

*Standard error of mean difference between B and A.
**Significant at 1% level.
†Not adjusted for age.

SEVERE LARGE VESSEL DISEASE

Severe large vessel disease was defined as coronary probable or amputation, or both, and was found in 14 patients, comprising nine men and five women. The mean (SD) age was 56·1 (11·0) years and mean (SD) duration of diabetes 10·8 (7·0) years (p<0·001 compared with those without large vessel disease). The mean (SD) serum cholesterol concentration was 4·26 mmol/l (1·17) and the mean (SD) high density lipoprotein cholesterol concentration 0·95 mmol/l (0·19). Six of the men and three of the women were hypertensive. The mean (SD) systolic blood pressure was 163·3 mm Hg (28·3) and the mean diastolic 86·3 mm Hg (10·6). The former was higher (p<0·01) than those without severe disease, but there was no difference in the latter.

INTERMEDIATE LARGE VESSEL DISEASE

Intermediate disease was defined as coronary possible or angina, or possible infarction or intermittent claudication, or any combination. This was found in 134 patients (22%), comprising 69 men (18·5%) and 65 women (28·5%).

Discussion

Hypertension was the main cause of large vessel disease in this series of diabetic patients. Although the mean systolic blood pressure was not always significantly higher in patients with cardiac, cerebral, or peripheral vascular disease, a high proportion were taking hypotensive drugs. Altogether, 235 (39%) patients were hypertensive, and this was commoner in women (100 of 228; 44%) than men (135 of 372; 36%). Both men and women with hypertension were more obese than those who were normotensive (men: mean 3·0, 95% CI 2·2 to 3·8; t=6·98, df=370, p<0·001; women: mean 3·9, 95% CI 2·5 to 5·3; t=5·65, df=226, p<0·001). Of these patients, 164 (70%) were taking hypotensive drugs but only 59 (36%) were normotensive when examined, and there was no difference in systolic or diastolic pressure between those who were taking hypotensive drugs and those who were found to be hypertensive. The commonest treatment for hypertension was a combination of methyldopa and thiazide diuretic (64 patients; 39%), while 34 (21%) patients were taking a diuretic and 34 methyldopa alone. The remaining patients were taking various combinations of β blocker, methyldopa, diuretic, and hydralazine.

Of the control subjects, 82 (17·5%) were hypertensive, and 18 (22%) of these were being treated, 10 with a thiazide diuretic alone, four with methyldopa, three with a combination of the two, and one with a β blocker. Comparing the diabetic patients aged 35 or over with controls, 228 (48·6%) diabetics were hypertensive against 82 (17·5%) control patients ($p<0·001$).

The concentrations of total serum cholesterol and high density lipoprotein cholesterol were uniformly low even in patients with severe large vessel disease, reflecting consumption of a diet low in saturated fats. Smoking was also not important. The overall prevalence of cigarette smoking was low (10%), and in the group with severe large vessel disease a few were smokers compared with over three quarters who were non-smokers. The age of the patient was not important in patients with peripheral vascular disease, but patients with cerebrovascular disease, the men who were coded coronary probable, and the women coded coronary possible were all statistically significantly older. Duration of diabetes was important only for men coded coronary probable. The long duration of diabetes in patients with severe large vessel disease probably reflects the inclusion of this group. There was no difference in body mass index in men or women between those with large vessel disease and those without.

When these results were compared with those of the WHO Multinational Study[1] the prevalence of severe large vessel disease in diabetics in Central Africa was comparable to that in diabetics in Hong Kong and Tokyo, who had the lowest prevalence of the countries studied. The intermediate results for large vessel disease probably do not accurately reflect the true prevalence of macrovascular disease in Africa as they rely largely on the results of the questionnaire. Many positive answers, especially from women, were probably due to misunderstanding the question. In the WHO study a similar wide variation was found in the frequency of positive answers to questions relating to large vessel disease, compared with the objective finding of electrocardiographic changes.

More women than men in every participating centre in the WHO study were coded "coronary possible." This was also the case here, but the difference was not significant, although women had higher rates of angina pectoris than men ($p<0·02$). Non-diabetic women had a similar proportion of electrocardiograms coded coronary possible as the diabetic women, but there was a pronounced difference in the proportions of diabetic and non-diabetic men with this coding, although no significant difference in age.

The Minnesota coding technique was designed for comparing populations and is not specific for coronary artery disease, especially in patients coded coronary possible with S-T segment and T wave abnormalities. Hypertension, pericardial or lung disease, infection, or metabolic disturbances may all produce non-specific changes. Race may also have an effect. For example, Walker and Walker found a higher prevalence of inverted T waves with S-T depression and diphasic T waves in young Bantu patients compared with white patients.[17] Prineas and Blackburn found changes in T waves more common in patients in Fiji and New Guinea, where there was virtually no other evidence of coronary artery disease, than in Australia and Tecumseh, Michigan, USA, where the rates of heart disease were high.[18]

Previous reports on electrocardiographic changes in African diabetic patients reflect the lack of standardised techniques in assessing these and the effect of different criteria used to select patients. For example, Chukwuemeka *et al* found that 15·6% of 198 Kenyan diabetics had ischaemic heart disease, but they excluded heavy cigarette smokers and patients with anaemia and hypertension (undefined),[3] while Osuntokun *et al* found that 11% of 556 Nigerian diabetic patients had an abnormal electrocardiogram, mainly left ventricular hypertrophy and strain pattern associated with hypertension, but they considered that only five patients had myocardial ischaemia compatible with coronary artery disease.[5] Mhando and Yudkin, however, had electrocardiograms from 139 Tanzanian diabetic patients subjected to Minnesota coding by the same two observers as in the present study.[9] They reported 5% as coronary probable and 18% as coronary possible. Seven of these patients, however, were aged under 30 and therefore unlikely to have ischaemic heart disease, and no control subjects were used.

Taking those patients with definite disease (coronary probable, amputation, or stroke) and those who replied affirmatively to the questionnaire and had electrocardiographic changes, only 8·6% of men and 7·5% of women had large vessel disease—that is, 8·2% overall. This is likely to be a more accurate estimate of the prevalence of macrovascular disease in patients with diabetes in Central Africa. Despite the high prevalence of hypertension large vessel disease was uncommon, which probably reflects the generally low serum cholesterol concentrations and few cigarette smokers.

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What limitations to physical activity are there for a person who has received an acrylic lens implant?

On the day after cataract surgery patients are ambulatory, and they return home soon afterwards. During the first six weeks after surgery the concern of the surgeon is for the integrity of the cataract wound, and the patient must be careful not to rub the eye. Driving, light shopping, walking, and desk work may be undertaken after this period. Then, assuming that there have been no complications, normal social and sporting activities may be reintroduced. After three months jogging, tennis, golf, and swimming can be enjoyed, but water polo, boxing, karate, and rugby are probably best stopped.—BRUCE NOBLE, consultant ophthalmic surgeon, Leeds.