A Survey of the Management, Control, and Complications of Diabetes Mellitus in Patients Attending a Diabetes Clinic in Blantyre, Malawi, an Area of High HIV Prevalence

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Abstract. The aim of this study was to describe the current status of diabetes care in an urban diabetes clinic in Malawi and the prevalence of human immunodeficiency virus (HIV) in this population, investigating possible associations between HIV and diabetes. A systematic prospective survey of patients attending the diabetes clinic at a teaching hospital in Blantyre, Malawi was conducted. Six hundred twenty patients were assessed. Seventy-four percent had glycosylated hemoglobin (HbA1C) > 7.5%. Systolic blood pressure was > 140 mm Hg in 52% of patients. Hypertension was more common in patients with raised creatinine ($P < 0.003$), retinopathy ($P = 0.01$), and stroke ($P < 0.0002$). Microvascular complication rates were high, specifically nephropathy (34.7%), retinopathy (34.7%), and neuropathy (46.4%). HIV seroprevalence was 13.7%. HIV-positive subjects had a lower body mass index (BMI) and lower fasting blood sugar, and they were more likely to have albuminuria (48.0% versus 33.3%; $P < 0.05$). Control of glycemia and hypertension were poor, and microvascular complications were common. Nephropathy in diabetic patients may be affected by HIV status.

INTRODUCTION

Surveys of the global burden of disease indicate that non-communicable diseases will become the leading cause of mortality worldwide by 2030.¹ Cardiovascular diseases make a significant contribution to that burden, and the risk factors of diabetes and hypertension are important determinants in the amount of cardiovascular disease.² Diabetes is increasing in prevalence, especially in developing countries, largely because of urbanization and epidemiological transition.³ In preparation for the increase in cases of diabetes, service development is a priority. To develop better services for diabetic patients, it is important to document the current situation of diabetes care.

Poor glycemic control is associated with worse diabetic outcomes, particularly the development and progression of diabetic complications.^{4–7} A number of surveys of diabetic control and complications have been published from sub-Saharan Africa.^{8,9} These surveys show many of the problems associated with managing diabetes in a resource-poor setting, including poor glycemic control and high prevalence of complications. Malawi is a small country in southeast Africa from which there is little published information about the management and complications of diabetes.

The overall prevalence of human immunodeficiency virus (HIV) infection in Malawian adults aged 15–49 years is 12%, with rates in urban adults of 17% (<http://www.unaids.org/en/CountryResponses/Countries/malawi.asp>). There are many potential interactions between HIV and diabetes mellitus. The two conditions have symptoms in common, such as weight loss and susceptibility to infection, particularly fungal infections like oral candidiasis. HIV itself and the drugs used to treat it, particularly the non-nucleoside reverse transcriptase inhibitors (NNRTIs) stavudine and lamivudine, which are first-line antiretroviral treatments (ARTs) in Malawi, can cause the metabolic syndrome that leads to development of new diabetes or deterioration in glycemic control in existing diabetic patients.¹⁰ Peripheral neuropathy is common in HIV-positive

patients in Malawi¹¹ because of direct HIV effects or treatment with stavudine, and therefore, in diabetic patients with neuropathy, it is not always apparent whether this is caused by diabetic neuropathy or HIV. Likewise, HIV-associated nephropathy (HIVAN) presents with proteinuria and may resemble diabetic nephropathy clinically.¹² It is, therefore, extremely important for optimal diabetes management to know which diabetic patients also have HIV. The prevalence of HIV infection in adult diabetic patients in an area of high HIV prevalence has not been described.

The aims of the survey were to describe the current status of diabetes care in a specialist diabetes clinic in a large African hospital, assess the prevalence of HIV among adult patients attending this clinic, and investigate associations of HIV and diabetes in this population.

MATERIALS AND METHODS

Setting. Queen Elizabeth Central Hospital (QECH) in Blantyre is the only teaching hospital in Malawi. It provides secondary care to the population of greater Blantyre (approximately 1 million) and tertiary care to the southern region of the country (approximately 5.9 million). The diabetic clinic at QECH represents the most specialized care available in the public sector and has been running for over 10 years. Patients are reviewed on a quarterly basis. All outpatient care is provided free in government health-care facilities. However, the only measure of control is a fasting blood-glucose measurement on clinic day. Measurement of lipids, glycosylated hemoglobin, and urine test sticks for microalbuminuria are not available. Diabetic medications regularly available free of charge are glibenclamide and insulin (lente and soluble). Metformin is available from private pharmacies locally but only rarely from the hospital pharmacy.

Subjects. A prospective cross-sectional survey was performed in the diabetes outpatient clinic at QECH, Blantyre, Malawi. Data were collected on consecutive patients attending the adult diabetes clinic for routine review between March and June 2007. The study had ethical approval from the Malawi College of Medicine Research and Ethics Committee (protocol number P.05/06/459). Informed consent was obtained from all patients before enrollment.

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Clinical assessment. A self-reported questionnaire was completed with the assistance of a research assistant. Data were collected on demographic variables, medications prescribed, dispensed, and taken, knowledge of HIV status, and disease understanding. Dietary adherence was assessed by asking about three indicators: (1) taking sugar in drinks/porridge, (2) drinking sobo/sprite or other sweet drinks, and (3) eating white nsima (highly refined maize flour, the staple carbohydrate eaten in Malawi). Details of relevant past medical history were obtained by questioning patients and referencing the health passport carried routinely by all patients in Malawi in which clinicians record details of each attendance at a health-care facility. Type 1 diabetes was defined based on young age at onset and early use of insulin.

Physical examination was undertaken by a trained clinician who was a member of the study team. Systolic (SBP) and diastolic (DBP) blood pressures,¹³ body mass index (BMI), and visual acuity were recorded. Neurovascular assessment of the feet was performed using an abridged four-point monofilament examination¹⁴ with a 10-gauge monofilament. Joint-position sensation and vibration sensation using a 128-Hz tuning fork were recorded. Objective sensory loss was defined as reduction in vibration, Joint position sense (JPS), or monofilament at the great toe in either foot. The presence of dorsalis pedis, posterior tibial pulses, and foot ulceration using the Wagner score¹⁵ were recorded. An ophthalmologist examined patients for the presence of diabetic eye disease and graded according to criteria used in the Liverpool Diabetes Eye Study.¹⁶ Slit lamp examination with 78 or 90 D was performed after pupil dilatation using tropicamide 1% ophthalmic solution or phenylephrine 10% eye drops. If treatable abnormalities were detected, patients were offered further intervention when possible.

Laboratory tests. Patients came in early on the morning of their clinic appointment for fasting blood sugar (FBS) measurement. For the purpose of the study, glycosylated hemoglobin (HbA1C) was performed using the Micromat II system (Bio-Rad, CA). All patients were tested anonymously for HIV. As per Malawian national policy, HIV status of study participants was confirmed using two standard rapid immunoassays (Uni-Gold Recombigen HIV and Determine HIV-1/2), and where discordant results were obtained, a third test using a different test kit was performed. Patients gave consent for HIV testing to be performed and were offered the opportunity to have voluntary counseling to learn the result of the test.

In a second phase of the study from October 2007 to February 2008, additional funding became available that allowed screening for renal disease. Patients attending the clinic were tested for microalbuminuria using Alburtis (Bayer, Tarrytown, NY) according to manufacturer's guidelines, and serum creatinine was measured. Because of population mobility, not all subjects were included in both surveys. For those only included in the second study, age, gender, FBS, BMI, SBP, and DBP measurements and antihypertensive medication were recorded. Because of lack of resources at this time, HIV testing and HbA1C measurement were not performed in this group, and not all demographic details were recorded.

Statistical analysis. Data were entered into a secure database and analyzed using StatView. Descriptive statistics (mean, standard deviation [SD], and range) were used to characterize the dataset. χ^2 tests were used to test between group differences for categorical variables, and the Mann-Whitney test was used for continuous variables.

RESULTS

Overall, there were 620 participants. Data are available for 481 participants in the main study; 526 had renal function measured, including 139 for whom data from the main study were unavailable.

Demographics. Basic demographic data are presented in Table 1; 18% were considered to have Type 1 diabetes. The mean BMI in patients with Type 1 diabetes was 24.5 (SD = 4.9; range = 14–39), and the mean BMI in patients with Type 2 diabetes was 28.7 (SD = 5.8; range = 15–48; $P < 0.0001$).

Management of diabetes. The mean FBS was 182.7 mg/dL (SD = 92; range = 11.6–580); 196 subjects (31.8%) had FBS within the target range of < 130 mg/dL, 301 (48.9%) had FBS of 130–260 mg/dL, and the remaining 119 (19.3%) had FBS ≥ 260 mg/dL. Inadequate glycemic control was also reflected by the HbA1C values: mean = 9.4% (SD = 2.5; range = 5–19.6). The distribution of HbA1C was $< 7.5\%$ $N = 114$ (25.6%), 7.5–10% $N = 150$ (33.7%), and $\geq 10\%$ $N = 181$ (40.7%). FBS and HbA1C were positively correlated ($r^2 = 0.187$; $P < 0.0001$).

The most recent treatment recorded in the patients' health passport was diet only (4%), glibenclamide monotherapy (37%), metformin monotherapy (1%), glibenclamide + metformin (27%), insulin (29%), and insulin + metformin (1%). However, although metformin was prescribed for 141 patients, only 95 (67%) had taken it because of non-availability.

TABLE 1
Demographics of the study population of patients attending the diabetes clinic

	First study			Second study	Entire cohort
	Whole cohort (N = 481)	Renal data available (N = 387)	Renal data not available (N = 94)	Renal data only (N = 139)	Total (N = 620)
Age (years)*	53.2 (14.0)	52.7 (13.6)	54.9 (15.7)	50.1 (14.5)	52.2 (14.1)
Gender; female (%)	289 (60.2)	240 (62.0)	49 (52.7)	78 (56.2)	316 (60.1)
BMI*	28.1 (5.9)	28.3 (5.8)	27.2 (6.0)	26.9 (5.6)	27.8 (5.7)
Duration of DM (years)*	7.0 (6.6)	7.0 (6.5)	7.0 (7.1)	NA	Only in first study
Education					
None	30	23	7	NA	Only in first study
Primary	212	174	38	NA	Only in first study
Secondary	204	162	42	NA	Only in first study
Tertiary	32	26	6	NA	Only in first study
FBS (mg/dL)*	187.1 (93.4)	188.3 (94.4)	182.1 (89.3)	167.2 (85.4)	182.7 (92.0)
HbA1C (%)*	9.4 (2.5)	9.4 (2.4)	9.4 (2.6)	NA	Only in first study

* Mean and SD reported. NA = not available. Of 481 patients in the first study, 387 had renal function assessed. Those who had renal function measured did not differ from the group as a whole.

Participants were asked how many times in the past year they had been unable to collect their medication from pharmacy; 220 (46%) had always been able to collect their drugs, but 141 (30%) had been unable to collect some part of their diabetes medication (usually metformin) on at least three occasions in the previous year. Of those who had been unable to get their medication, 69 had no means to buy medication from private pharmacies and therefore had gone without it.

Of the subjects who were on insulin treatment, 82 stored it in a refrigerator, 33 stored it in a clay pot to keep it cool because they had no access to a refrigerator,¹⁷ and 32 used neither a clay pot or refrigerator. Twenty-seven of 145 patients were noted to have a poor insulin injection technique, and 5 of 145 had problems with their injection sites.

On the whole, metformin was prescribed for subjects with higher BMIs (average BMI of those prescribed metformin was 29.7 and average BMI of those not prescribed metformin was 27.4); however, of the 112 subjects with BMI ≥ 30 , only 65 (58%) were prescribed metformin.

A simple questionnaire about disease understanding and dietary adherence indicated that 150 of 478 subjects stated they did not understand what diabetes was and 328 of 478 stated they would like more education. Only 262 of 478 subjects (55%) were complying with appropriate diet.

Management of hypertension. Data on blood pressure (BP) and hypertension management were available for 526 subjects. In the whole sample, including those on antihypertensive medication, 273 (52%) had SBP ≥ 140 mm Hg, and 220 (42%) had DBP ≥ 90 mm Hg. Two hundred fifty-three patients were taking antihypertensive medication, and the majority of these still had uncontrolled hypertension (Table 2). Paradoxically, the greater the number of prescribed antihypertensives, the worse the BP control. The most frequently prescribed antihypertensive was methyl dopa ($N = 147$) followed by hydrochlorothiazide ($N = 49$), angiotensin converting enzyme inhibitor (ACEI) ($N = 46$), β blocker ($N = 45$), hydralazine ($N = 23$), nifedipine ($N = 18$), and other ($N = 9$).

Macrovascular complications. The major macrovascular complication of diabetes is cerebrovascular disease. No patients had documented computerised tomography scan results, but based on self-report and the health passport, 35 of 478 had had a stroke. Twenty-one of these took regular aspirin. Stroke patients were significantly older (59.6 versus 52.6 years; $P = 0.002$); 31 were taking antihypertensive medication, and 3 had untreated hypertension. Despite treatment, stroke patients had higher BP (SBP = 154 versus 138 mm Hg, $P < 0.0002$; DBP = 89 versus 82 mm Hg, $P < 0.01$).

Peripheral vascular disease (PVD) was indicated by the absence of arterial pulses in the feet. In 36 of 474 subjects, the dorsalis pedis pulses were absent on one or both sides. No patients had symptoms suggestive of PVD.

No subjects were known to have ischemic heart disease (IHD) or had symptoms suggestive of IHD. Further investigation

to identify asymptomatic heart disease was not possible. Only three subjects in the entire clinic population admitted to being current or former smokers.

Microvascular complications. *Nephropathy.* 181 of 522 (34.7%) subjects had $\geq 1+$ albuminuria, suggesting probable diabetic nephropathy, and 57 (10.9%) had 2+ albuminuria or greater. Of those with heavy albuminuria $\geq 3+$ ($N = 25$), 13 had raised creatinine (≥ 1.2 mg/dL), and 18 were on antihypertensive treatment but BP control was inadequate; only four patients had BP $< 130/80$ mm Hg. Those with albuminuria were more likely to have raised creatinine. Ninety-seven of 526 (18.4%) participants had raised creatinine ≥ 1.2 mg/dL, 12 (2.3%) had creatinine ≥ 2.0 mg/dL, and 2 had creatinine ≥ 7 mg/dL, signifying likely end-stage renal disease. The presence of albuminuria was associated with duration of diabetes and HIV positivity but not glycemic control (FBS or HbA1C), BP, or age. There was a strong association between creatinine and SBP, age, and duration of diabetes and a weak negative association between creatinine and FBS (Table 4). ACEI use in nephropathy patients was infrequent; only 4 subjects with albuminuria and 14 with raised creatinine were taking ACEIs.

Neuropathy. Symptoms of peripheral neuropathy were common; 222 of 478 (46.4%) reported foot numbness, and 157 of 475 (33.1%) had objective evidence of sensory loss. There was a strong association between self-reported numbness and objective sensory loss ($\chi^2 = 20.7$; $P < 0.0001$). Those with objective evidence of neuropathy were significantly older and had a longer duration of diabetes, higher SPB, and worse glycemic control as indicated by FBS but not HbA1C. Sensory loss was significantly associated with ulcers and amputation (Table 3). Thirty-eight of 480 (8%) had amputations or current ulcers, and the Wagner scores of the ulcers were $N = 14$ for grade 0, $N = 12$ for grade 1, $N = 5$ for grade 2 or 3, and $N = 1$ for grade 4.

Retinopathy. Two hundred seventy-four patients underwent ophthalmological assessment; 95 (34.7%) had any retinopathy, and 67 (24.5%) had sight-threatening eye disease (STED). The associations of retinopathy are shown in Table 4. Retinopathy was significantly associated with longer duration of diabetes, higher SBP, higher FBS (but not HbA1C), raised creatinine, presence of albuminuria, and presence of sensory loss. Two hundred fifty-seven participants had visual acuity (VA) measured with correction. The VA in the best eye of each subject revealed that 144 (56%) had normal vision (metric VA = -0.176 – -0.176), 94 (36.6%) were partially sighted (metric VA = 0.301 – 0.778), and 19 (7.4%) had registerable blindness (metric VA = 1 – 2.9). Thirty-six patients had cataracts, and they were bilateral in 33 of those patients.

Effects of HIV. HIV testing was carried out on 475 subjects. Sixty-five (13.7%) tested positive. Of these, only 16 were aware of their status, 11 of whom were taking ART. Those who tested HIV positive did not differ from those who were HIV negative in age or gender. HIV-positive subjects had a lower BMI and lower FBS, although not a lower HbA1C (Table 5).

TABLE 2

Number of antihypertensive drugs prescribed versus BP measurement

No antihypertensive drug prescribed	No. of subjects	No. of patients with SBP ≥ 140 mm Hg (%)	No. of patients with DBP ≥ 90 mm Hg (%)
0	271	88 (32.4)	72 (26.6)
1	189	131 (69.3)	109 (57.7)
2	57	46 (80.7)	33 (57.9)
3	7	7 (100)	5 (71.4)

TABLE 3

Association of foot ulcers and amputation with the presence of neuropathy

	Neuropathy present ($N = 157$)	Neuropathy absent ($N = 318$)	P
Current foot ulcers	19/157 (12.1%)	13/318 (4.1%)	< 0.001
Previous amputation	7/157 (4.5%)	3/318 (0.09%)	< 0.014

TABLE 4
Factors associated with microvascular complications

Risk factor	Complication											
	Albuminuria			Raised creatinine			Retinopathy			Neuropathy		
	≥ 1+ (N = 181)	< 1+ (N = 342)	P	> 1.2 mg/dL (N = 98)	≤ 1.2 mg/dL (N = 428)	P	Present (N = 95)	Absent (N = 179)	P	Present (N = 157)	Absent (N = 318)	P
Age (years)	51.8	52.5	0.9	58.4	50.8	< 0.0001	54.5	52.3	0.2	56.6	51.3	0.0004
Duration of DM (years)	7.3	5.7	< 0.05	9.3	5.6	< 0.0001	9.7	5.1	< 0.0001	8.1	6.5	< 0.03
FBS (mg/dL)	179.1	170.9	0.16	160.5	177.0	< 0.04	206.9	180.7	< 0.03	204.0	178.4	< 0.02
HbA1C (%)	9.6	9.3	0.3	9.4	9.2	0.5	9.4	9.4	0.7	9.6	9.3	0.12
SBP (mm Hg)	147.6	141.8	0.09	152.0	141.8	< 0.003	145.5	136.0	0.01	151.3	140.6	0.001
DBP (mm Hg)	87.3	86.3	0.5	89.1	86	0.14	83.8	81.5	< 0.15	90.0	85.4	< 0.01
HIV-positive	24/135 (17.8%)	26/248 (10.5%)	< 0.05	10/72 (13.9%)	41/315 (13.0%)	0.8	10/94 (11%)	25/177 (14%)	0.4	24/155 (15.5%)	410/315 (12.7%)	0.4
Creatinine > 1.2 mg/dL	55 (30%)	43 (12.6%)	< 0.0001	—	—	—	21/81 (26%)	17/158 (4%)	< 0.003	27/119 (22.7%)	44/264 (16.7%)	0.2
Albuminuria ≥ 1+	—	—	—	54 (55.7%)	126 (29.6%)	< 0.0001	40/83 (48%)	41/155 (26%)	< 0.001	49/134 (35.6%)	69/246 (28.0%)	0.09

TABLE 5
Comparison of HIV-positive and -negative subjects

	HIV negative (N = 410)	HIV positive (N = 65)	P
Age (years)	53.4	51.0	0.1
Female gender	247 (60.2%)	41 (63%)	0.7
BMI	28.3	26.8	< 0.015
HbA1C (%)	9.5	9.0	0.1
FBS (mg/dL)	193.2	153.4	< 0.001
SBP (mm Hg)	139.6	136.2	0.1
DBP (mm Hg)	82.9	80.7	0.3
Albuminuria ≥ 1+	111/333 (33.3%)	24/50 (48.0%)	< 0.05
Creatinine ≥ 1.2 mg/dL	62/336 (18.5%)	10/51 (19.6%)	0.8
Retinopathy	84/236 (35.6%)	10/35 (28.6%)	0.4
Neuropathy			
Subjective numbness	184/408 (45.1%)	36/65 (55.4%)	0.1
Objective sensory loss	131/406 (32.3%)	24/64 (37.5%)	0.4

HIV positivity was associated with albuminuria but not raised creatinine. Binary logistic regression showed that HIV was an independent risk factor for proteinuria, and the odds ratio of having proteinuria in those with HIV was 2.0 (95% confidence interval [CI] = 1.1–3.8). There was no significant difference in the frequency of retinopathy or neuropathy.

DISCUSSION

We present the largest prospective survey of a diabetic clinic population in resource poor sub-Saharan Africa. This is the first study to report specifically on HIV prevalence in an outpatient diabetes clinic in the region and describe the particular features associated with HIV in this group.

At the time that the survey was carried out, the clinic was not using any protocols or guidelines, and diabetes management and complication screening was left to the discretion of the clinicians. Likewise, there were no diabetes nurses, and patient education was given by the doctors during the consultation. Nearly three-quarters of patients had HbA1C measurements above 7.5%. The lack of protocols and guidelines in the clinic may well have resulted in poor management, but a number of other factors that may contribute to suboptimal control are shown in our data. Twenty-nine and a half percent of patients reported that drugs prescribed were unavailable in the hospital pharmacy. As well as leaving patients without effective treatment, this was likely to have an effect on prescribing practice. Clinicians were aware that some drug classes were frequently unavailable and were likely to prescribe inferior regimens based on the drugs that they expected to be dispensed. This is particularly true of metformin, which, although recommended as first-line treatment in Type 2 diabetes in the International Diabetes Federation (IDF) 2005 Global Guideline for Type 2 Diabetes, was under-prescribed and often unavailable. At the time of the study, metformin was only listed as a second-line drug for diabetes management in The Malawi Standard Treatment Guidelines (MSTG). These guidelines are used as a national formulary and determine what drugs are available in the government stores. After this study, the treatment guidelines have been updated, with metformin as first-line treatment, and supplies are improving. Insulin was available most of the time, but incorrect usage may have played a role in poor control. A large number of patients did not refrigerate their insulin (although most who did not have access to a refrigerator did store their insulin in a clay pot, which may be of some use in temperature reduction¹⁷),

and there was a subgroup identified who did not use the correct injection technique. Knowledge and understanding about diabetes and diabetic diet was poor, and a large proportion of patients did not comply with diabetic diet.

Hypertension was common and badly controlled. It is well-established that poor BP control in diabetic patients results in worse outcomes and that hypertension is a significant risk factor for the development of complications.^{4,18} In keeping with this, we found higher levels of uncontrolled hypertension in patients with a history of stroke, increased creatinine levels, and retinopathy. Our data show an inverse relationship between the number of antihypertensive drugs prescribed and good BP control. This suggests that clinicians were aware that patients were hypertensive, because they prescribed more antihypertensive drugs for those individuals, but this did not lead to better control. There are a number of possible explanations for this. First, certain antihypertensive agents are more effective than others, particularly in black populations^{19,20}; however, this was not reflected in prescribing practice in the clinic. In keeping with the MSTG in use at that time, methyldopa was the most commonly prescribed antihypertensive, whereas nifedipine was the least commonly prescribed. Second, as with hypoglycemic agents, intermittent availability of drugs results in poor adherence to prescribed regimens. Third, there was no system for review of hypertension between quarterly visits to the diabetes clinic. Thus, through a combination of poor glycemic and hypertensive control, our patients are at particular risk of complications.

Historically, macrovascular disease in diabetic patients in Africa has been uncommon, despite high rates of hypertension, but these rates may be increasing.⁷ In our population, 7.3% reported stroke, the prevalence of foot ulceration was 6.7%, and there were low rates of peripheral vascular disease. These rates are comparable with previous studies in Africa.²¹ Very few patients took aspirin, although this is usually available. Low rates of smoking may partly explain the low incidence of macrovascular complications, particularly peripheral vascular disease. Stroke is the main manifestation of macrovascular disease, and previous studies published indicate that ischemic infarcts represent 58% of acute strokes²² in Malawi. Good management of the diabetic foot is crucial if ulceration and amputation are to be avoided, but it is notoriously difficult in settings such as this where many walk barefoot or have inappropriate footwear. There are, however, simple interventions that can improve foot care even in resource-limited settings,²³ and efforts should focus on education of both health-care providers and patients.

Microvascular complications were common, with 34.7% having abnormalities consistent with nephropathy, 34.7% having retinopathy, and 46.4% having probable neuropathy. The prevalence of retinopathy in our study is comparable with other studies from Africa that report rates of 14–53%.^{8,9,24–27} Although the rate of STED in South Africa has been reported as 11%,²⁴ which is much lower than the rate in our population, other studies in sub-Saharan Africa from outside South Africa have not described STED separately. Before this study, visual acuity checks and annual fundoscopy were not routine for patients attending the clinic, and there was no service for diabetic retinopathy management, although this has since been instituted. Management should continue to focus on improving early detection and preventing by risk-factor control and access to treatment of established retinopathy.

As with other studies from the West and Africa, the presence of probable nephropathy was associated with longer duration

of diabetes, systolic hypertension, and older age.^{8,28,29} The mean age in our study population was higher than in some other series reported from Africa, and this may explain the higher prevalence of renal disease in our cohort. There are a number of particular difficulties in managing renal disease in Malawi. Diagnostic and monitoring laboratory investigations are not routinely available, pharmacological treatments are inadequate, renal replacement therapy is accessible to only a handful of patients living in the capital city, and renal transplant is not available. A new observation that we made is that, in the subgroup of diabetic patients with renal disease, the presence of albuminuria is associated with being HIV positive.

The prevalence of HIV in this cohort is comparable with the urban adult population in Malawi, but most who tested HIV positive in our study were not aware of their status. The presence of albuminuria was the only abnormality found more commonly in HIV-positive patients. HIV can directly affect the kidney, giving rise to HIVAN, which can also present as proteinuria. Studies from America have clearly shown that HIVAN is predominantly found in black patients,^{30,31} and it is likely to play an important role in HIV-positive patients in Africa. It is, therefore, possible that HIVAN may have been contributing to proteinuria in some of our patients. A recent study has reported on the association of non-HIV factors in predicting proteinuria in HIV-positive patients. The study by Gupta and others³² showed that, in a large cohort of HIV-infected patients with a diabetes prevalence of 8%, proteinuria was associated with diabetes and hypertension as well as HIV-related factors.³² The prevalence of renal disease in African patients affected by both HIV and diabetes has not been well-studied. In fact, a recent large study of HIV-infected patients with proteinuria performed in South Africa specifically excluded patients with diabetes.³³ Another study in which renal biopsies were performed on HIV-positive patients in South Africa found that 2 of 99 patients had evidence of diabetic nephropathy.³⁴ Both patients were known to be diabetic, but the authors do not report the prevalence of diabetes in their cohort.³⁴ Although nephropathy is common in both conditions, it is not known whether HIV infection and diabetes have a synergistic effect in the kidney to cause or accelerate progression of renal disease. Our data do go some way in supporting this theory, although further investigation is required.

Peripheral neuropathy in both diabetes and HIV is common.¹¹ Distal predominantly sensory symmetrical polyneuropathy (DSSP) is the most common form of peripheral neuropathy in late-stage HIV infection, and diabetes is a recognized risk factor.^{35,36} Although the presence of subjective numbness, the most common feature of DSSP, was higher in the HIV-positive subgroup, this was not statistically significant. Numbers in this group, however, were small, and the association may have become significant with greater numbers of patients. A recent multicenter study examined a group of HIV-positive patients with both sensory neuropathy and metabolic syndrome.³⁷ The authors found that type 2 diabetes mellitus and elevated levels of serum triglycerides, but not other components of the metabolic syndrome, were significant risk factors for peripheral neuropathy.³⁷ The mechanism for this interaction remains unclear.

It is well-established that HIV is associated with the development of a metabolic syndrome that can result in impaired glucose tolerance and diabetes. Although there is now a large body of research on the metabolic syndrome found in HIV,

this evidence has been gathered in Western settings.^{38,39} The effects of HIV on insulin resistance and diabetes in patients living in Africa are not known. It is notable that HIV-positive patients in this cohort had lower BMIs and lower FBS measurements than HIV-negative patients with diabetes; it is possible that this may influence the course of their diabetes, but it has not been well-described elsewhere. The lower average BMI of African patients, traditional African lifestyle and diet, and lower rates of smoking may all affect the metabolic profile of these patients, and Western data may not be reliably extrapolated to these populations.

The role of ART in the development of a metabolic syndrome and lipodystrophy is well-recognized both in developed countries and Africa.^{40,41} Increasing numbers of patients on HIV treatment may result in a new group of patients with insulin intolerance and abnormalities of lipid metabolism.⁴² The low number of patients on ART in our study means that we are unable to comment on the effects of HIV treatment in this cohort, and larger studies are needed.

We recognize the limitations of our study. First, the study was conducted in a single central hospital. The clinic population was mainly urban dwellers and those referred for specialist advice, and therefore, our results cannot be extrapolated to other settings. Diabetes management in rural areas is likely to be even less satisfactory. A second potential bias is that the service is seen by many as a clinic for collecting medication, and so, patients with diet-controlled diabetes are almost certainly underrepresented. Third, some of our data relied on self-reporting or information carried in the health passport, and therefore it may be inaccurate.

Our data show that the management of diabetes was poor and that complication rates were high. We have subsequently introduced clinic guidelines and protocols based on the IDF guidelines and nurse-led education classes. A revised version of the MSTG has also been produced. Our findings raise questions about the interaction between HIV and diabetes in this setting. Resources in countries such as Malawi are limited, and some feel that non-communicable diseases are neglected, particularly in the face of the devastation that HIV has brought to the region. There has been a misconception by some that the HIV epidemic will result in fewer people living long enough to develop diseases such as diabetes. However, population-modeling studies in South Africa have shown that, even with the reduction in population caused by HIV, there will be significantly more people living with diabetes because of the dramatic rise of diabetes prevalence over the next decades.⁴² These models may even have underestimated the numbers living with HIV and diabetes, because they did not take into account the increased numbers of people on HIV treatment with the rollout of ART programs. This will both increase the survival of HIV-positive people and increase their risk of developing diabetes.

The African Diabetes Declaration 2006 calls for “a truly integrated approach which utilizes the whole health workforce to address infectious and non-communicable diseases simultaneously,” but the management of patients with diabetes in Africa, and particularly the subgroup who are also infected with HIV still remains a challenge. To improve the current situation, there needs to be a focus on improving the delivery of health care to patients with diabetes by conducting regular operational research and evaluating the impact of implementing practice guidelines. Before the HIV epidemic, chronic

disease management was not a priority for African countries. However, the Malawian model of ART rollout may provide a model for the scaling up of diabetes care. ART provision is free to all patients in Malawi, and there has been a highly successful scale up of ART using the public-health approach. Many of the principles of chronic disease management that have been applied to HIV and ART can also be applied to the management of diabetes. Through the use of simple protocols and an emphasis on monitoring and evaluation, we hope to develop a service that provides standards of care consistent with international guidelines and is responsive to change. Further information is desperately needed on the interactions between HIV, ART, and diabetes in sub-Saharan Africa, as the prevalence of diabetes increases alongside the HIV epidemic in the region.

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