Table V. Incidence of ventricular arrhythmia events at baseline, 3 months, and at end of study (number of patients)

	Hydrochlorothiazide (*N* = 15)	Indapamide (*N* = 15)
VPB < 10/hour		
Baseline	12	13
3 months	2	12
VPB 10 - 30/hour		
Baseline	9	1
3 months	3	3
VPB > 30/hour		
Baseline	8	1
3 months	0	2
Couplets		
Baseline	0	0
3 months	0	0
Non-sustained VT		
Baseline	0	0
3 months	1	1

VPB = ventricular premature beats; VT = ventricular tachycardia.

thiazide dose from 12.5 to 25 mg daily did not have any additional significant effect on BP, but worsened the hypokalaemia. Therefore, based on these results, indapamide may be an appropriate choice of antihypertensive diuretic therapy in black South African patients with mild to moderate hypertension. Both study medications were well tolerated, with no serious adverse events or deaths observed. However, serum potassium levels should be monitored throughout therapy with both diuretics and potassium supplementation should be given where necessary.

We have referred to black patients as this was our study population at Chris Hani-Baragwanath Hospital. Patients of African descent respond differently to Caucasians when given antihypertensive medication, and this is well documented in the literature. As black patients suffer more from the effects of hypertension — end-stage renal failure, heart failure, etc. — it is important to determine causes and optimal treatment in this high-risk group both in South Africa and other populations elsewhere (e.g. African-Americans).

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DIABETES IN RURAL SOUTH AFRICA — AN ASSESSMENT OF CARE AND COMPLICATIONS

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Objectives. To describe the diabetic population under care of the public health sector in a district in rural KwaZulu-Natal, to assess the nature of their care, their glycaemic control and the extent of their complications.

Subjects and methods. Two hundred and fifty-three diabetic patients consecutively attending clinics for review were interviewed and examined, and where available a 12-month retrospective review of clinical records was performed. Random blood glucose, haemoglobin A_{1c} (HbA_{1c}) and urine albumin/creatinine ratio were assayed.

Results. Acceptable glycaemic control (HbA_{1c} < 2% above normal population range) was found in only 15.7% of subjects (95% confidence interval (CI): 11.4 - 20.8%). Mean HbA_{1c} was 11.3%. The prevalence of hypertension (blood pressure ≥ 160/95 mmHg and/or prescribed antihypertensive medication) was 65.4% (CI: 59.0 - 71.1%). Of 129 patients who were prescribed antihypertensives, 14.0% (CI: 8.5 - 21.2%) were normotensive (< 140/90 mmHg). Severe obesity was present in 36.5% (CI: 30.4 - 42.9%). Rates of attendance for review and compliance with diabetic medications were high. Blood glucose monitoring was not regularly performed and medications were rarely modified. Complications were common and mostly undiagnosed. Retinopathy of any grade was found in 40.3% of patients (CI: 33.2 - 50.9%) and was severe enough to warrant laser photocoagulation in 11.1% (CI: 8.5 - 21.2%). Microalbuminuria was found in 46.4% (CI: 40.0 - 53.0%) and foot abnormalities attributable to diabetes in 6.0% (CI: 3.4 - 9.7%).

Conclusions. Care and control of diabetes in this rural community is suboptimal. There is a need for primary care staff to focus on modifying prescriptions in the face of poor blood glucose control and/or uncontrolled hypertension. Additional training and support for nursing staff and education for patients will be central to achieving this level of intervention.

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The World Health Organisation (WHO) estimates that there are 150 million people with diabetes worldwide, a figure that is expected to double by the year 2025.[1] Until recently it was considered to be rare in sub-Saharan Africa, but as a result of demographic and lifestyle changes, as well as increasing recognition, it is being identified as a major health problem.[2] In urbanised black populations in South Africa, recent surveys estimate the prevalence of diabetes at around 8% in those over 30 years of age[3,4] and it is a major cause of mortality and morbidity.[5-7]

Ongoing quality care is necessary to minimise the incidence and severity of acute and chronic complications. Evidence-based standards of care and specific treatment targets centred on the long-term control of blood glucose and hypertension have been formulated[8] and adapted for the situation in South Africa.[9] However, the management of diabetes in the light of studies supporting intensive intervention is complex and delivering anything like ideal care presents enormous problems.[10] This is especially true in rural areas where particular socioeconomic, cultural and geographical difficulties exist. So far, studies in South Africa have focused on urban diabetic populations[3,7,11] and little is known about the quality of care and distribution of complications in rural communities.

The aim of this study was to describe the diabetic population under the care of the government health sector in Hlabisa, a typical health district in rural KwaZulu-Natal, to assess the nature of the care they receive, the level of blood glucose control achieved and the extent of complications.

SETTING

Hlabisa district has a population of around 200 000, most living in scattered, rural homesteads. Prevalence data for total diabetes are not yet available in Hlabisa, or elsewhere in rural southern Africa. Electronic data linkage of lists from the hospital and peripheral clinics identified 302 registered patients (whole population crude prevalence rate of 0.2%)[12] but a large majority almost certainly remain undiagnosed.[13]

Government health care is provided at a 300-bed district hospital. In addition there is a mobile clinic service, and 12 permanent clinics staffed by nurses trained in primary health care and visited by a doctor on a monthly basis. The management of diabetes is nurse-led and centres on algorithms designed to be used by experienced primary care nurses to implement stepwise treatment for diabetes and concurrent hypertension.[14] Patients are requested to attend each month.

SUBJECTS AND METHODS

Over a 2-month period in 1999, consecutive diabetic patients presenting for follow-up at the hospital and the district's permanent clinics were given their next appointment on one of a series of specific days as close to their normal monthly appointment as possible. This approach was calculated to maximise recruitment.

Interview and record review

Participants were interviewed by a single physician and a nurse translator using a structured protocol. Socio-demographic data were recorded. Duration of diabetes and a history of diabetic complications and treatment were confirmed where possible by consulting patient-held records. The number of follow-up visits attended, abnormal clinical observations or biochemical results, medications and interventions in the previous 12 months were taken from the records. Patients were asked about their compliance with diabetic and hypertensive medications, using sample tablets for comparison.

Examination

Weight, height and blood pressure (BP) were measured by an experienced nurse. BP was measured at the right antecubital fossa, seated, using an appropriately sized cuff. Readings above 140/90 mmHg were repeated after 5 minutes and the lowest diastolic and systolic values recorded.

Feet were examined by the physician for signs of ulceration, infection, amputation and absence of dorsalis pedis pulses. Peripheral neuropathy was not assessed.

Visual acuity was measured using a Snellen chart at 6 m with distance correction if glasses were worn. Slit-lamp biomicroscopy of the anterior segment was performed by an ophthalmologist. Objective refraction by retinoscopy was performed in those with visual acuity < 6/18 and clear media. Indirect stereoscopic fundoscopy was performed at the slit-lamp through dilated pupils.

Biochemical tests

Venous blood samples were taken for determination of albumin/creatinine ratios, haemoglobin A_{1c} (HbA_{1c}) and random blood glucose (RBG) levels. HbA_{1c} was measured using a Roche Cobas Integra high-performance liquid chromatography assay (non-diabetic 95% reference range of 4.5 - 5.7%, interassay coefficient of variation of 0.82%). Fresh urine samples were tested with reagent strips for the presence of proteinuria.

Data management and statistical methods

Double-entered data were stored in Epi Info 6 and analysed using Stata 6. Proportions are followed in parentheses by 95% exact binomial confidence intervals (CIs), unadjusted for sampling fraction. Chi-squared and Student's *t*-tests were used to test the significance of differences in discrete and continuous variables respectively. Predictors of chronic diabetic complications were examined by univariate analysis (χ^2 testing) and stepwise multivariate logistic regression.

Definitions

For the purposes of this study, type 1 diabetes was defined by onset of insulin dependency under 40 years of age or a history of ketoacidosis. All other patients with diabetes were labelled as type 2 even if they were insulin-treated.

Patients receiving antihypertensive medication or with a repeat systolic BP ≥ 160 mmHg or repeat diastolic BP ≥ 95 mmHg were defined as hypertensive. Borderline hypertension was diagnosed if BP ≥ 140/90 mmHg but < 160/95 mmHg.[15,16]

Obesity was defined as a body mass index (weight/height^2) above 27 kg/m^2 and severe obesity as above 33 kg/m^2.

Renal function was assessed using the urine albumin/creatinine ratio. Microalbuminuria was defined as a value above 2.5 mg/mmol in men or 3.5 mg/mmol in women, and macroalbuminuria as a ratio ≥ 20 mg/mmol.[17]

Visual impairment was classified according to WHO and International Classification of Diseases (ICD)-10 definitions in which low vision was defined as a visual acuity < 6/18 but ≥ 3/60 in the better eye, and blindness was defined as a visual acuity <3/60 in the better eye.[18] Diabetic retinopathy was classified and graded according to the guidelines of the Early Treatment Diabetic Retinopathy Study Research Group (ETDRS),[19,20] according to the findings in the most severely affected eye.

RESULTS

Demographic and social

The study population consisted of 253 Zulu diabetic patients representing 83.8% of the registered diabetic population in the district.[12] The mean age ± standard deviation (SD) was 56.5 ± 10.4 years (range 21 - 81 years), and 26.9% were male. The excess of females is an accurate reflection of the patients attending for chronic medical care in Hlabisa.[14] Of 68.4% of patients not old enough to receive an old-age pension, only 12.7% were employed, 56.0% were unemployed and 27.7% received a state disability grant. The median years of schooling was 4 (interquartile range 0 - 7 years).

Type and duration of diabetes

Eighteen patients (7.1%) were insulin-dependent (type 1) diabetic patients. Of the 235 (92.9%) non-insulin-dependent (type 2) subjects, 28 (11.9%) were insulin-treated and 3 (1.2%) were diet-controlled. The period since diagnosis displayed a log normal distribution with a geometrical mean of 4.2 years (range 6 weeks - 60 years).

Glycaemic control

HbA_{1c} was assayed in 98.4% of the study population. The mean ± SD was 11.3 ± 3.0% (range 5.2 - 21.9%) A value within the normal population range (4.5 - 5.7%) was found in only 2

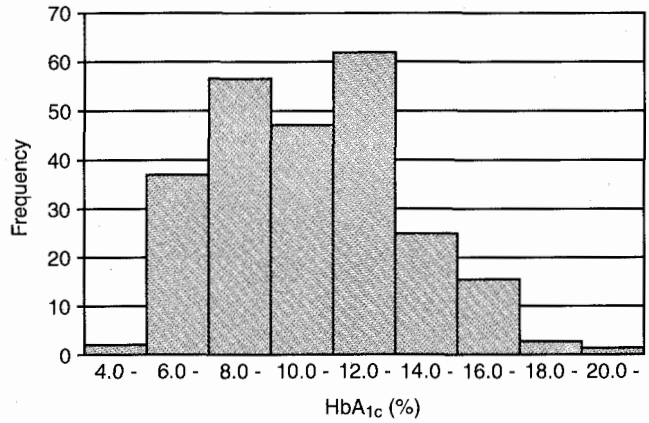

Fig. 1. Frequency distribution of HbA_{1c}.

patients and 84.3% (79.2 - 88.6%) had an HbA_{1c} over two percentage points above this upper limit. The frequency distribution is shown in Fig. 1. The mean HbA_{1c} in patients with type 1 diabetes (11.9%) and type 2 diabetes (11.2%) were not significantly different ($P = 0.32$). The mean ± SD RBG was 14.5 ± 7.5 mmol/l. A value below 4.0 mmol/l was found in 1.6% (0.4 - 4.0%), and 66.3% (60.2 - 72.2%) had a value over 10.0 mmol/l.

Hypertension

Hypertension was present in 165 subjects (65.4%, 59.0 - 71.1%) of whom 78.2% (71.1 - 84.2%) were currently prescribed antihypertensive medications. Borderline hypertension was found in a further 40 subjects (15.8%). Among those prescribed antihypertensive medication, 14.0% (8.5 - 21.2%) were normotensive (BP < 140/90 mmHg), 41.8% (33.2 - 50.9%) had a BP ≥ 140/90 mmHg but < 160/95 mmHg, and 44.2% (35.5 - 53.2%) had a BP ≥ 160/95 mmHg. Recent guidelines recommended a target BP < 130/85 mmHg for diabetic patients.[21,22] This target was only met in 19.8% (15.0 - 25.2%) overall, and 10.1% (5.5 - 16.6%) of those on medication.

Compliance with antihypertensive medication (reported taking medication in the previous 24 hours) was 61.2%.

Compliance with diabetic medication

Among both insulin-dependent and non-insulin-dependent patients, 94% reported having taken their medication in the previous 3 days. This extended period was chosen because it was known that some diabetic patients omit their medication on the day of clinic attendance.

Body mass index

The mean ± SD body mass index (BMI) was 31.2 ± 6.9 kg/m^2 (range 17.1 - 60.4 kg/m^2). Obesity (BMI > 27 kg/m^2) was present in 63.0% of subjects (56.6 - 69.2%), and 36.5% (30.4 - 42.9%) were severely obese (BMI > 33 kg/m^2). The mean was

significantly higher in women (32.0 kg/m²) than men (29.1 kg/m²) ($P = 0.003$).

Diabetic complications

One hundred and seventeen subjects (46%) had been admitted to hospital on at least one occasion for a complication related to diabetes.

Ophthalmic. Diabetic retinopathy of any grade was present in at least one eye of 40.3% (34.2 - 46.6%) of the 251 subjects (99.2%) in whom fundoscopy was performed. The proportion in the small number of insulin-dependent patients (52.6%, 28.9 - 75.6%) was not significantly different ($P = 0.18$). The distribution according to the grade of retinopathy in the worse eye is given in Table I. In 5.6% of subjects (3.1 - 9.2%) retinopathy had progressed to the proliferative stage, with 42.8% of those patients already blind or at high risk of severe visual loss in at least one eye.[23] Macular oedema was found in 16.2% (7.5 - 15.7%) of patients, and in 10.3% (6.8 - 14.7%) this was clinically significant.[24] Overall, 11.1% (7.5 - 15.6%) of patients required retinal photocoagulation to reduce their risk of progression to severe visual loss according to recommended guidelines.[23,24] Pan-retinal photocoagulation had been performed in 3 of the 14 subjects with proliferative retinopathy, 2 of whom required further treatment because of persistent retinal ischaemia. Four subjects were blind, 2 as a result of diabetic retinopathy. Visual impairment was found in 12.3% of subjects (8.5 - 16.9%), the main contributors being cataract and refractive errors.

Table I. Frequency of diabetic retinopathy by type and grade

	Number	%	95% confidence for %
Nonproliferative			
Minimal	37	14.7	10.6 - 19.7
Moderate	34	13.5	9.6 - 18.4
Severe/v.severe	16	6.3	3.7 - 10.1
Proliferative	14	5.6	3.1 - 9.2
Maculopathy			
All cases	41	16.2	11.9 - 21.3
Clinically significant	26	10.3	6.8 - 14.7
All retinopathy	102	40.3	34.2 - 46.6

Renal. An elevated urine albumin/creatinine ratio was present in 46.4% (40.0 - 53.0%) of subjects and 13.4% (9.3 - 18.4%) had macroalbuminuria. The reagent strip tests revealed proteinuria in 23.3% (18.0 - 29.4%) on the study day but we were unable to comment on the level of persistent proteinuria since too few patients had had repeated urine testing recorded in the notes.

Peripheral vascular. Dorsalis pedis pulses were absent in 16.6% of patients (12.2 - 21.8%). Signs of foot ulceration or cellulitis were present in 6.0% (3.4 - 9.7%) and 1 patient had had multiple surgical toe amputations. No cases of dry gangrene were seen.

Cerebrovascular. A history consistent with cerebrovascular accident was elicited from 7.5% of subjects (4.6 - 11.5%).

Medical attention in the previous year

Patient-held medical records were available for review in 236 cases (93.3%). Among those who had been diagnosed and under local care for at least 12 months (90.2%), the mean number of visits ± SD in the previous year was 9.5 ± 3.4 (range 1 - 18). BP was recorded at least once in 86.9% (81.9 - 90.9%) of the sets of notes but monitoring of glycaemia was less frequent: 47.6% (40.6 - 54.6%) had no blood glucose recorded, 77.8% (72.1 - 82.8%) had no urine glucose monitoring and 43.7% (36.8 - 50.8%) had neither during the previous year. Only 7 patients monitored their diabetes themselves at home.

Among those with a recorded BP, 68.3% had at least one reading > 140/90 mmHg and 50.2% had two or more high recordings. In those with a recorded blood glucose reading, 66.6% had at least one reading ≥ 17 mmol/l and 32.5% had two or more. However, despite these abnormal results, few changes to medication were made. Of 118 cases with at least two abnormal BP or blood glucose readings only 28 had their medication altered (23.7%, 16.4 - 32.4%).

Six patients had had dilated fundoscopy recorded in the previous 12 months.

Predictors of complications

There was a strong tendency for coexistence of different forms of microangiopathy. Subjects with retinopathy were more likely to be microalbuminuric or macroalbuminuric (unadjusted odds ratios 4.2 (2.3 - 7.6) and 5.5 (2.3 - 13.4) respectively).

On multivariate logistic regression, retinopathy was also found to be positively associated with increasing length of time since diagnosis, age, and HbA_{1c}, and negatively with increasing BMI. Those with diabetes diagnosed at least 5 years previously were at six times greater risk than more recently diagnosed patients, and those aged over 50 years were more than three times likely to have retinopathy than younger subjects. The significance of glycaemic control as measured by HbA_{1c} as a risk factor for retinopathy was only marginal, although an isolated assay reflects mean glycaemia only for the last 2 months. Women were nearly three times more at risk than men after adjusting for other factors, possibly reflecting increased vascular mortality in males. Increasing BMI was associated with a large reduction in risk — by a factor of five in the severely obese. No effect of hypertension or type of diabetes was apparent, although the small number of insulin-dependent patients is acknowledged. Details of the analysis are given in Table II.

Risk factors for microalbuminuria as the outcome of interest were slightly different (Table III). The trend for increased risk

Table II. Risk factors for diabetic retinopathy

Predictors	No. of cases (%) (*N* = 253)	No. with retinopathy (%) (*N* = 102)	Odds ratio (95% CI) from logistical regression*	*P*-value†
Duration (yrs)				
≤ 5	130 (54.1)	30 (12.5)	–	
5 - 10	52 (21.7)	30 (57.7)	6.1 (2.7 - 13.5)	< 0.001
> 10	58 (24.2)	37 (63.8)	6.0 (2.7 - 13.0)	< 0.001
BMI (kg/m²)				
≤ 27	65 (27.0)	37 (56.9)	–	
27 - 33	88 (36.5)	31 (35.6)	0.28 (0.12 - 0.64)	0.002
> 33	88 (36.5)	31 (35.2)	0.20 (0.08 - 0.48)	< 0.001
Age (yrs)				
≤ 50	67 (26.9)	17 (25.7)	–	
51 - 60	97 (39.0)	45 (46.9)	3.5 (1.5 - 8.4)	0.004
> 60	85 (34.1)	37 (43.5)	3.3 (1.3 - 8.1)	0.009
HbA_{1c} (%)				
≤ 8.0	42 (16.9)	9 (22.5)	–	
8.1 - 11.0	77 (30.9)	34 (45.3)	2.9 (1.0 - 8.1)	0.045
11.1 - 14.0	86 (34.5)	36 (41.9)	2.3 (0.82 - 6.4)	0.11
> 14.0	44 (17.7)	21 (47.7)	3.4 (1.1 - 11.2)	0.041
Gender				
Female	185 (73.1)	79 (43.6)	–	
Male	68 (26.9)	23 (33.8)	0.37 (0.17 - 0.82)	0.014

* Model contains duration of diabetes, body mass index (BMI), HbA_{1c}, age and gender. No significant interaction terms. Odds ratios compared with first category as baseline.
† Chi-squared test.
BMI = body mass index; CI = confidence interval.

Table III. Risk factors for microalbuminuria

Predictors	No. of cases (%) (*N* = 253)	No. with micro-albuminuria (%) (*N* = 140)	Odds ratio (95% CI) from logistical regression*	*P*-value†
Duration (yrs)				
≤ 5	130 (54.1)	59 (45.0)	–	
5 - 10	52 (21.7)	30 (56.6)	1.49 (0.73 - 3.04)	0.27
> 10	58 (24.2)	37 (76.7)	4.19 (1.93 - 9.10)	< 0.001
BMI (kg/m²)				
≤ 27	65 (27.0)	45 (69.2)	–	
27 - 33	88 (36.5)	49 (55.7)	0.49 (0.22 - 1.09)	0.079
> 33	88 (36.5)	39 (44.3)	0.27 (0.08 - 0.48)	0.002
Age (yrs)				
≤ 50	67 (26.9)	38 (56.7)	–	
51 - 60	97 (39.0)	52 (53.6)	0.77 (0.37 - 1.61)	0.50
> 60	85 (34.1)	49 (57.6)	0.65 (0.29 - 1.44)	0.29
HbA_{1c} (%)				
≤ 8.0	42 (16.9)	17 (40.5)	–	
8.1 - 11.0	77 (30.9)	39 (50.6)	1.57 (0.66 - 3.73)	0.31
11.1 - 14.0	86 (34.5)	49 (57.0)	1.99 (0.86 - 4.64)	0.11
> 14.0	44 (17.7)	32 (72.7)	4.69 (1.65 - 13.3)	0.004
Hypertension				
No	88 (34.8)	96 (58.2)	–	–
Yes	165 (65.2)	44 (50.0)	2.11 (1.07 - 4.17)	0.031

* Model contains duration of diabetes, body mass index (BMI), HbA_{1c}, age and hypertension. No significant interaction terms. Odds ratios compared with first category as baseline.
† Chi-squared test.
BMI = body mass index, CI = confidence interval.

with longer duration and higher HbA_{1c} is demonstrated, albeit only reaching significance for those diagnosed for more than 10 years or in the worst category of glycaemic control. Severely obese subjects were nearly four times less likely to be microalbuminuric than those with normal BMI. Those with definite hypertension were at twofold increased risk compared with normotensives but age, gender and insulin dependence were not significant.

Discussion

Glycaemia control in this group of rural patients was poor. Only 15.7% achieved the target level for HbA_{1c} of < 2% above the normal population range set in national guidelines for managing diabetes in primary care.[24] This compares badly with results from clinic-based studies not only in industrialised countries[25-27] but also elsewhere in Africa[7,28] and places this population at significant risk of increased morbidity and mortality. Contributing to this risk was the high proportion of patients with hypertension.[22] Nearly two-thirds of subjects were hypertensive by our definition (≥ 160/95 mmHg or prescribed antihypertensive medication); however, a stricter target of < 130/85 mmHg is now widely recommended in diabetes[21,22] and this was only met by 1 in 5 subjects. The proportion with hypertension is higher than reported in other diabetic populations.[7,25,29] This may in part be because of the 'white coat' effect, as we only used readings on a single day, and an element of misdiagnosis in those on treatment cannot be discounted. But it may also be a reflection of the very high levels of obesity in South African type 2 diabetic patients[7] compared with elsewhere in Africa[30] — two-thirds had a BMI > 27 kg/m².

The prevalence of chronic complications was also high. Retinopathy of any grade was found in 40.3% of subjects while in 11.1% the retinal appearance warranted laser photocoagulation. Few patients had undergone fundoscopic examination and nearly all retinopathy was previously undiagnosed. Nearly half of the subjects had evidence of renal damage in the form of a high albumin/creatinine ratio which is known to predict progression to renal failure.[31] Foot abnormalities attributable to diabetes, including ulceration, sepsis and surgical amputation were found in 6%.

Several independent risk factors for developing microvascular complications reported in non-Africans[27,32-35] were confirmed, most notably duration of diabetes. A strong negative association was found with increasing BMI, a similar finding to that reported in Hong Kong and Zambia[30,36] for nephropathy and neuropathy. It is possible that this could reflect confounding by socioeconomic status, on which we did not collect data, or alternatively it may represent residual confounding from the effect of poor glycaemia control since

hyperglycaemia is known to result in weight loss as well as microvascular disease. A single assay for HbA_{1c} as performed in this study does not necessarily reflect control over several years.

Reported microvascular complication prevalences in sub-Saharan Africa have varied widely.[2,6,7,30,37-39] This may be partly a result of different diagnostic criteria, duration of disease and selection biases inherent in this type of prevalence study. Attendance at diabetic clinics is dependent on motivation, resources and mobility and as a result this type of study is likely to over-represent the wealthier, better-educated and least disabled of diabetics in the community. These complication rates also reflect survival. Mortality is high in African diabetes[40] and many patients may die before developing complications or die prematurely as a result of them.

The study attempted to identify causes of poor diabetic control. Patient compliance was good, reflected by clinic attendance for review, and knowledge of and adherence to prescribed treatment. Several areas of service provision were suboptimal. Local guidelines do not encourage regular blood glucose monitoring in the clinic, but even where this was performed very few results were acted upon. Similarly, although most patients had their BP monitored, few of those with repeated high readings had had their treatment modified. As a result, the majority of patients remain inadequately treated.

Diabetes has been targeted as a disease requiring special attention in South Africa and the importance of a community-based primary care approach has been emphasised. This study demonstrates that there is still a long way to go to achieve acceptable standards of care for diabetic patients in this rural community. There is a need for health care workers to focus on implementing existing protocols particularly with regard to changing prescribing in the light of evidence of poor blood glucose control. Additional training and support for nursing staff and education for patients[41] will be central to achieving this and a specialist nurse educator is to be introduced in the district to try to co-ordinate this.

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