II. Course and prognosis

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Abstract

***Objective*—To determine the clinical course of diabetes mellitus in tropical Africa.**

***Design*—Continuing care and follow up until 31 March 1989 of all newly diagnosed diabetic patients registered at one hospital between 1 June 1981 and 31 May 1987.**

***Setting*—Muhimbili Medical Centre, Dar es Salaam, Tanzania.**

***Subjects*—1250 Newly diagnosed diabetic patients seen over a six year period. 272 (21·8%) Had diabetes requiring insulin, 825 (66·0%) diabetes not requiring insulin, and 153 (12·2%) diatetes of uncertain type.**

***Main outcome measures*—Survival rates during each year of follow up.**

***Results*—205 (16·4%) Patients were known to have died, 126 (61·5%) in hospital and 79 (38·5%) in the community. At least a further 71 patients were likely to have died. The five year survival rates (95% confidence intervals) for patients with diabetes requiring and not requiring insulin were 71% (62% to 80%) and 84% (80% to 89%) respectively for known deaths and 60% (51% to 69%) and 82% (77% to 86%) respectively for known plus probable deaths. 49 (3·9%) Patients died at the time of presentation. Severe diabetic ketoacidosis and infection were responsible for most deaths in patients with diabetes requiring insulin. Infection was responsible for 24% of deaths in patients with diabetes not requiring insulin and was the main cause of death in the group with uncertain type of diabetes. Cardiovascular and renal causes were responsible for 24% of hospital deaths of patients with diabetes not requiring insulin. Diabetes requiring insulin, young age, and ketonuria at presentation were associated with a significantly worse five year survival on multivariate analysis. On univariate analysis underweight, female sex, low educational background, and manual occupations were additional factors with a worse prognosis.**

***Conclusion*—Diabetes in sub-Saharan Africa is, in many patients, a serious disease with a poor prognosis. Most deaths, however, are due to preventable causes. More effort is therefore required to increase public awareness of diabetes and to improve patient detection, management, and follow up.**

Introduction

An observation made in Tanzania in 1964 that the fate of diabetic patients was "obscure"[1] remains largely true throughout the African continent. The 1985 report of the World Health Organisation study group on diabetes stated, for example, that, "In developing countries where insulin and medical supplies are scarce, IDDM [insulin dependent diabetes mellitus] patients are known to die young for want of treatment, although evidence to support this claim is poor."[2] Studies of diabetic patients in tropical Africa have often referred to the problem of patient follow up,[1 3-6] and in only one study from Zimbabwe have most patients in a cohort of 107 newly diagnosed patients admitted to hospital been successfully followed up six years after diagnosis.[7] No studies have yet described the clinical course and prognosis for patients with non-insulin dependent diabetes. This study reports the clinical course and outcome of diabetes in 1250 newly diagnosed diabetic patients seen over a six year period in Dar es Salaam and after a follow up period ranging from 22 to 94 months.

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Patients and methods

The setting, patients, data recorded on registration, and diagnosis and classification of patients have been described in the previous paper. Basic information on all newly diagnosed diabetic patients was recorded, irrespective of mode of presentation, type of diabetes, and whether the patient was admitted or not. As obtaining an accurate address is often difficult in African cities—streets may have no names and houses no numbers—the name of the patient's ten cell leader was also recorded (a ten cell unit is the basic political-administrative unit in Tanzania and consists of 10 households with one elected leader). Throughout the period of follow up one of us attempted to visit the homes of those patients who had not attended the diabetic clinic for over six months. For patients living outside Dar es Salaam it was often possible to receive reports of progress from medical colleagues caring for them in other centres. Some patients also returned to Dar es Salaam for review.

Patients were reviewed until 31 March 1989. The period of follow up ranged from 22 to 94 months.

ASSESSMENT OF DEATHS

In addition to patients known to have died we estimated the number of patients lost to follow up who were likely to have died. Assessment of the likelihood of death was based on, for example, discharge of patients with gangrene against medical advice or young patients admitted with diabetic ketoacidosis who did not return for insulin and whose general condition was known to be poor.

Information on deaths in the community was obtained from following up patients in the community and voluntary reports by patients' relatives. Whenever possible relatives were asked about the patient's condition before death and the circumstances leading up to death.

DATA ANALYSIS

Five year survival rates were estimated separately for each type of diabetes and also for all patients irrespective of the type of diabetes. The Kaplan-Meier product limit technique was used in the survival time analysis, as outlined by Armitage and Berry[9] and Machin and Gardner.[10] The log rank test[9 10] was used to calculate the hazard ratio and its 95% confidence interval to estimate differences in survival rates between two groups. To determine which factors were associated with survival, non-dichotomous variables were grouped into two groups with the lower group marked off as follows: age <30 years, body mass index <20 kg/m^2, symptom duration <four weeks. Peasant farmers (including manual workers) and office workers were each tested against all other occupations. Ketonuria was grouped

as either present or absent (nil or trace). Patients without formal education were compared with those with at least some primary education. Body mass index, hypertension, and smoking and drinking habits were defined as described in the previous paper. Patients who died before discharge on the first admission or not seen after the first visit were excluded from the analysis to determine factors associated with survival. The Cox proportional hazards model[9] was used for a multivariate survival time analysis, using the analysis module (Pecan) of the Egret statistical package version 0.22.4 (Statistics and Epidemiology Research Corporation, Seattle, United States).

Results

MORTALITY

Until 31 March 1989, 205 (16·4%) of the 1250 patients were known to have died, 126 (61·5%) in hospital and 79 (38·5%) at home or in the community. At least a further 71 patients (5·7%) were likely to have died, 30 in the group with diabetes requiring insulin, 19 in the group not requiring insulin, and 22 with uncertain type of diabetes. Thus about 22% of all patients may have died.

Figure 1 shows survival curves for the total population and for the three diagnostic categories, and figure 2 shows survival curves based on known and probable deaths. The five year survival rate (95% confidence interval) based on known deaths was 71% (62% to 80%) for patients with diabetes requiring insulin, 84% (80% to 89%) for patients not requiring insulin, and 55% (35% to 75%) for patients with diabetes of uncertain type. If survival rates are based on known plus probable deaths the five year survival rate was 60% (51% to 69%), 82% (77% to 86%), and 43% (25% to 60%) respectively. For the total population the five year survival rate was 78% (73% to 82%) based on known deaths and 71% (66% to 76%) if based on known plus probable deaths.

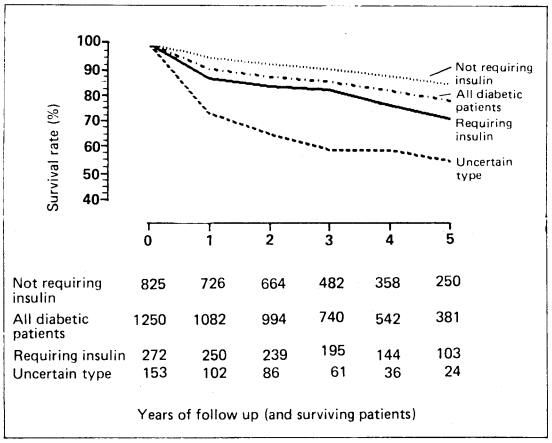

Fig 1—Survival rates of diabetic patients based on number of patients known to have died. Effective sample sizes at time zero and for each year of follow up are given for each group

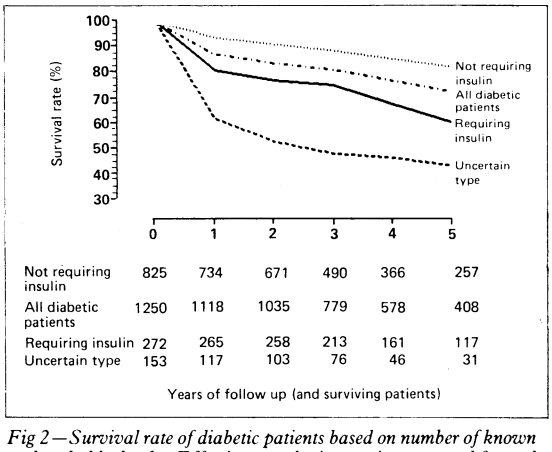

Fig 2—Survival rate of diabetic patients based on number of known and probable deaths. Effective sample sizes at time zero and for each year of follow up are given for each group

TABLE I—*Causes of death of 126 diabetic patients known to have died in hospital in Dar es Salaam, Tanzania*

	Type of diabetes		
	Requiring insulin	Not requiring insulin	Uncertain
No (%) dying of:			
Diabetic coma (ketoacidotic, hyperosmolar)	19 (50)	1 (2)	
Hypoglycaemia	2 (5)	1 (2)	3 (12)
Infection:			
Of extremities (including gangrene and septicaemia)	3 (8)	12 (19)	7 (28)
Tuberculosis and other chest infections	6 (16)	2 (3)	5 (20)
Diarrhoeal diseases	3 (8)	1 (1)	
Cardiovascular and renal diseases		15 (24)	1 (4)
Liver disease	1 (3)	5 (8)	3 (12)
Cancer		10 (16)	1 (4)
Miscellaneous		5 (8)	1 (4)
Unknown	4 (11)	11 (18)	4 (16)
Total	38 (100)	63 (100)	25 (100)

TIME OF DEATH

Mortality was highest in the six months after presentation. Forty nine patients died at the time of presentation and a further 38 within the following six months. Thirty (79%) of the 38 deaths occurred in the community. This was partly due to the discharge of very rich patients back into the community, but many of the deaths were in patients with diabetes requiring insulin, suggesting that the early months of disease may be particularly dangerous for young patients receiving insulin. Of the 272 patients with diabetes requiring insulin, 18 (6·6%) died on admission as did 17 (2·1%) of the 825 patients not requiring insulin and 14 (9·2%) of the 153 patients with uncertain type of diabetes. Thus 49 (3·9%) of the 1250 patients died at the time of presentation.

CAUSES OF DEATH IN HOSPITAL

Table I shows the causes of death in hospital in the three groups of patients. Sixty two (23%) of the 272 patients with diabetes requiring insulin were admitted in severe diabetic ketoacidosis, 16 of whom (26%) died. A further three patients died of severe diabetic ketoacidosis on subsequent admissions, so that 19 (50%) of the 38 deaths in the patients requiring insulin were due to diabetic ketoacidosis. Twelve deaths (32%) were directly due to infections, including pulmonary tuberculosis and diarrhoeal diseases.

Of the 63 patients with diabetes not requiring insulin who died, one died as a result of hyperosmolar non-ketotic diabetic coma and one of drug induced hypoglycaemia. Fifteen (24%) deaths were due to infection and 15 (24%) to cardiovascular or renal causes. Cancer caused the death of 10 (16%) patients. Among the 25 patients with uncertain type of diabetes who died infection was the primary cause of death in 12 (48%).

Table II compares the causes of death in the entire population with those described in studies from the United States and Britain.[11 12]

CAUSES OF DEATH IN THE COMMUNITY

Most deaths in the 25 patients with diabetes requiring insulin seemed to be due to diabetic ketoacidosis or hypoglycaemic coma.

In patients with diabetes not requiring insulin three of the 29 patients who died were known to have cancer. Four patients died of stroke or congestive cardiac failure. A further three, one of whom had a hemiplegia,

TABLE II—*Causes of death of diabetic patients in Tanzania who died in hospital compared with causes of death of diabetic patients in United States[12] and United Kingdom[13]*

	Tanzania (all ages, 1981-7)	United States (all ages, 1960-4)	United Kingdom (age ≤50, 1979)
No (%) dying of:			
Diabetic coma (ketoacidotic, hyperosmolar)	20 (15·9	29 (1·1)	74 (16·5)
Hypoglycaemia	6 (4·8)	7 (0·3)	17 (3·8)
Infections (excluding chest infections)	26 (20·6)	154 (5·8)	9 (2·0)
Pulmonary tuberculosis and other chest infections	13 (10·3)	3 (0·1)	
Cardiovascular and renal diseases	16 (12·7)	2053 (77·9)	262 (58·5)
Liver disease	9 (7·1)	26 (1·0)	8 (1·8)
Cancer	11 (8·7)	249 (9·5)	33 (7·4)
Miscellaneous	6 (4·8)	106 (4·0)	45 (10·0)
Uncertain	19 (15·1)	7 (0·3)	
Total	126 (100·0)	2634 (100·0)	448 (100·0)

were hypertensive when last seen, and one had had a myocardial infarction and angina pectoris. One patient had ankle oedema, ascites, and albuminuria, and one had had a history of jaundice for three months when last seen. Two patients were known to have chronic otitis media and two a chronic cough when they last attended the clinic.

Among the 25 patients in the uncertain category who died in the community tuberculosis was the probable cause of death in four and other infections in five. Two patients were known to have chronic liver disease and two to have congestive cardiac failure.

LOSS OF PATIENTS FROM FOLLOW UP

Table III shows the number of patients definitely known to have died in each group and the number of patients in each diagnostic category seen in the six months before 31 March 1989. Of the patients with diabetes requiring insulin, not requiring insulin, and of uncertain type, 142 (68% of those known not to have died), 409 (56%), and 36 (35%) were seen or known to be alive in the six months before 31 March 1989. Of the 209 patients requiring insulin not known to have died, 163 (78%) were seen within the 12 months up to 31 March 1989, but 22 (11%) had not been seen or heard of for over three years. Of these 22 patients, 10 returned to up country towns where they could not be traced, and six were not seen after discharge from the ward. Of the 733 patients with diabetes not requiring insulin, 90 (12%) had not been seen or heard of for over three years, 19 of whom had returned to up country towns; 31 did not return for follow up after their first admission or first visit to the diabetic clinic.

The default rate was greatest among the 103 patients with uncertain types of diabetes. Forty five (44%) had not been seen for over three years, 34 of whom did not return even once after initial presentation, 11 because they had moved to a distant region. It is likely that up to half of this group of patients had died. Of the 1250 patients, 115 (9·2%) were not seen again after their initial presentation, 47 because they could not be traced in towns in other parts of Tanzania.

FACTORS ASSOCIATED WITH MORTALITY

In the survival analysis each variable was divided into two groups (age <30 years and ≥30 years). The survival rate for one group was compared with that of the other for each variable in: (*a*) all patients irrespective of treatment; (*b*) patients with diabetes requiring insulin; and (*c*) patients with diabetes not requiring insulin.

Table IV shows the variables significantly associated with survival when the patients were considered together. There were no significant differences for age, ketonuria at presentation, smoking, drinking, family history of diabetes, blood pressure, and duration of symptoms.

When the variables were analysed in the patients with diabetes requiring insulin significant differences were found for body mass index, as in all the patients combined. In addition, men with diabetes requiring insulin had a higher five year survival rate than women (83% *v* 66%; hazards ratio 2·5, 95% confidence interval 1·3 to 5·0).

For the patients not requiring insulin body mass index was again significantly associated with survival. The groups for occupation and education had significantly different survival rates. Office workers had a better prognosis than the rest (five year survival 94% *v* 84%; hazards ratio 2·4 (1·4 to 4·3)) and the manual workers and peasant farmers a worse prognosis (five year survival 82% *v* 88%; hazards ratio 1·9 (1·1 to 3·3)). Patients with no formal education fared worse than the rest (five year survival 82% *v* 90%; hazards ratio 2·4 (1·4 to 4·0)).

On multivariate analysis with the Cox proportional hazards model, and for all patients, both ketonuria (hazards ratio 0·77 (0·64 to 0·91)) and age (hazards ratio 0·55 (0·41 to 0·73)) were significant. Patients requiring insulin had a significantly worse survival than those not requiring insulin (hazards ratio 0·52 (0·35 to 0·74)). All other variables had insignificant hazards ratios.

TABLE III—*Diabetic patients known to have died and those known to be alive in the six months before 31 March 1989*

	Known to have died	Known to be alive
No (%) requiring insulin (n=272)	63 (23·2)	142 (52·2)
No (%) not requiring insulin (n=825)	92 (11·2)	409 (49·6)
No (%) with diabetes of uncertain type (n=153)	50 (32·7)	36 (23·5)
Total (n=1250)	205 (16·4)	587 (47·0)

TABLE IV—*Five year survival rates for variables with significant hazards ratios between groups*

Variable	No at time zero	Five year survival rate (%)	Hazards ratio (95% confidence interval)
Sex:			
Men	795	83	
Women	337	76	1·5 (1·0 to 2·1)
Occupation:			
Peasant farmers	302	76	
All others	729	84	1·9 (1·3 to 2·8)
Occupation:			
Office workers	217	90	
All others	814	79	1·9 (1·3 to 2·9)
Body mass index			
<20 kg/m²	264	65	
≥20 kg/m²	743	89	5·0 (3·3 to 7·5)
Education:			
Below primary	419	76	
Primary or higher	573	86	2·2 (1·6 to 3·2)
Type of diabetes:			
Requiring insulin	241	77	
Not requiring insulin	775	85	1·5 (1·0 to 2·2)
Type of diabetes:			
Requiring insulin	241	77	
Uncertain type	116	57	4·5 (2·6 to 7·7)
Type of diabetes:			
Not requiring insulin	775	85	
Uncertain type	116	57	13·2 (7·1 to 24·4)

Discussion

A study from Papua New Guinea found that diabetes was a "rapidly fatal and morbid disease" in that country.[13] Our study showed that the prognosis for diabetic patients in tropical Africa, even where facilities for care exist, is also much worse than for patients in developed countries. That this was likely to be so was suggested by previous studies reporting the loss of patients from follow up[1 3 6] and postmortem studies indicating that infection and acute metabolic complications were common causes of death.[14 15] In one follow up study from Zimbabwe in which the initial study population was clearly defined,[7] after six years 49 (46% of 107) patients were known to have died; nine (8%) died at the time of presentation. It is unlikely that this population was representative of the general diabetic population in Zimbabwe as three quarters were treated with insulin, almost one quarter had steatorrhoea, and

a high proportion were heavy drinkers.[16] Our study population, though hospital based, included most patients with symptoms who presented to clinics and hospitals in Dar es Salaam during the six year study period. To our knowledge no community based studies of the clinical course of diabetes have been reported from a developing country.

In Tanzania about two fifths of patients requiring insulin die five years after diagnosis, whereas in developed countries only one third die 30 years after diagnosis.[2] In Denmark, for example, 40% of patients with insulin dependent diabetes survive for more than 40 years.[17] For patients in developed countries with diabetes not requiring insulin life expectancy is, on average, several years less than that for people without diabetes, but few die within five years of diagnosis,[2] whereas in Tanzania at least 15% are dead within five years of diagnosis. Mortality among normal weight and underweight patients with diabetes not requiring insulin may be considerably higher; we believe that most patients with uncertain type of diabetes were probably normal weight and underweight patients with diabetes not requiring insulin.

Severe diabetic ketoacidosis was the cause of death in half the patients requiring insulin who died in hospital. Infection, including pulmonary tuberculosis, was the second major cause of death. In contrast, in Western countries most deaths among patients requiring insulin are related to cardiovascular and renal causes (table II). Among patients with diabetes not requiring insulin who died in hospital these cardiovascular and renal causes were responsible for only one quarter of all deaths, and infection was responsible for a similar proportion. Again, these findings contrast with those from developed countries, where most deaths in non-insulin dependent diabetic patients are due to cardiovascular and renal complications.[11] Liver disease seems to be a commoner cause of death in developing countries, and the proportion of patients dying from cancer is similar in both developing and developed countries.

Little is known about the course of most chronic diseases in Africa, mainly because of problems of patient follow up. This fact and the high mortality associated with many diseases must be viewed against the prevailing socioeconomic background. The problem of loss of patients from follow up is not unique to Africa,[18,19] but cultural and socioeconomic factors make the problems of caring for patients with chronic disease particularly difficult in poor countries. Patients may be unwilling to accept the concept of a disease for which there is no cure; their views on aetiology may be quite different from orthodox Western ones; and often they cannot afford to attend clinics regularly.

In the present study a special effort was made to keep track of patients, but even so many patients were lost to follow up. The worsening economic state of most people in tropical Africa makes it likely that attendance at follow up clinics will continue to be a problem.

It would be useful if patients at special risk of dying could be identified and care focused on them. Studies in the United States and Europe have identified factors in patients with insulin dependent diabetes associated with a favourable or a poor prognosis.[20-22] Our study also found factors associated with an increased risk of death, such as type of diabetes, low body mass index, younger age, female sex, poor educational background, manual occupations, and ketonuria at presentation. Two studies from Zimbabwe reported that consumption of alcohol was also associated with shorter survival.[7,23]

The interests of diabetic patients in developing countries may be best served by efforts to increase the awareness of the general public and traditional healers of the symptoms and signs of diabetes and its infective complications, including tuberculosis. Awareness of diabetes among health workers should also be increased and provision made for the widespread dissemination of easily understood and appropriate management plans for the care of diabetic patients. Most deaths are preventable, and with increased efforts more patients could be enabled to lead socially and economically productive lives. We have evidence that survival of patients seen in the later period of the study was improving, but continued improvement requires a sustained commitment on the part of medical staff, which is often difficult with so many competing demands. Our experience suggests that properly motivated paramedical staff are the key to providing continuing care and follow up of patients with chronic diseases like diabetes in developing countries.

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