Original Articles

Sources of Disparity in the Spectrum of Diabetes Mellitus at Incidence and Prevalence

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In a population-based study in Rochester, Minnesota, the clinical characteristics of 1135 patients newly diagnosed with diabetes (1945–69) were compared with those of 810 residents with diabetes mellitus on prevalence day (1 January 1970). The prevalence patients were older and the male:female ratio was reduced from that seen among incidence cases. The prevalence patients were more likely to be on oral agents, had lower fasting blood glucose levels, were less likely to be symptomatic, but were more likely to have macrovascular and microvascular complications. These differences seemed to come about as a result of variation in survival rates among patients with specific characteristics, differential migration of certain groups of patients, and changes in the status of individuals. DIABETES CARE 6: 427–431, SEPTEMBER–OCTOBER 1983.

Even a cursory review of the literature reveals a rather wide range of opinion on such fundamental aspects of diabetes epidemiology as the proportion of patients with insulin-dependent diabetes, the age and sex distribution of the disease, and the prevalence of retinopathy and other vascular complications. Many of the disagreements result from failure to account for inherent differences in the clinical spectrum of diabetes among patients seen at various points in the course of the disease or at different levels in the medical care system. The potential importance of these differences is frequently unrecognized because so few systematic studies of the problem have been undertaken. The purpose of the present report is to compare the clinical characteristics of patients at the initial diagnosis of diabetes (incidence cases, N = 1135) with those of surviving patients examined at a subsequent point in time (prevalence cases, N = 810), using data from the population-based study of diabetes mellitus among residents of Rochester, Minnesota. An attempt is made to identify some of the factors responsible for the differences observed.

METHODS

Details of the methods employed in the study of diabetes mellitus in the community of Rochester, Minnesota, have been described previously.[1] The diagnostic criteria used were those reported by Palumbo and co-workers.[2] These criteria were somewhat more generous than those proposed by the National Diabetes Data Group,[3] but we have shown that the differences have little practical effect on the apparent clinical spectrum of diabetes.[4] The criteria used resulted in an incidence cohort of 1135 Rochester residents newly diagnosed with diabetes between 1945 and 1969, while 810 diabetic patients who had met the criteria resided in Rochester on 1 January 1970.

The fasting blood glucose value used in this report for incidence cases was the first one for each patient that met the diagnostic criteria. For prevalence cases, the value closest to 1 January 1970 was taken. Fasting blood glucose levels were divided as recommended by West[5] into three categories: ≤199 mg/dl whole venous blood, 200–299 mg/dl, and ≥300 mg/dl. Patients who had glucose tolerance tests (GTT) diagnostic of diabetes but fasting whole blood glucose levels less than 110 mg/dl were labeled as "GTT alone." Fasting blood glucose levels were not available for 15 prevalence cases. Relative weight was calculated using recommended height-weight tables,[3] and patients were considered obese when relative weight was 1.2 or greater. Relative weight could not be assessed for two prevalence patients. Therapeutic regimens were classified as insulin (with or without other therapy), oral agents (with or without diet but without insulin), or diet alone (no insulin or oral agents) as of the time of discharge after the initial diagnosis and workup and on prevalence day. The characterization of specific clinical types of diabetes generally followed National Diabetes Data Group recommendations, although as explained in detail in a separate report some modifications were required in the

context of a retrospective study using existing medical records.[1] The clinical type of diabetes mellitus at prevalence could not be determined for three individuals. Diabetic "complications" were classified as macrovascular (angina pectoris, myocardial infarction, sudden unexpected death, stroke, transient ischemic attack, or peripheral vascular disease) or microvascular (retinopathy of diabetic renal disease). Complications at diagnosis and on prevalence day included a history of any one or more of these. Relative survival was determined using actuarial methods,[6] with death rates for West North Central whites 1960 as the standard. Actuarial methods were also used to estimate the cumulative incidence of macrovascular and microvascular disease. For the calculation of incidence and prevalence rates, the entire population of Rochester was considered to be at risk, and the denominator age- and sex-specific person-years (p-y) were derived from decennial census figures.

RESULTS

The crude incidence of diabetes mellitus in Rochester, Minnesota, over the entire study period, 1945–69, was 121.3 per 100,000 p-y (95% confidence interval: 114.2–128.4), based on the 1135 cases diagnosed. The crude prevalence of diabetes in Rochester on 1 January 1970 was almost 13 times greater at 1539.1 per 100,000 p-y (95% confidence interval: 1433.1–1645.1), based on 810 cases. The age- and sex-specific incidence and prevalence rates are compared in Table 1. In each instance the rates increased with age, but the statistically significant ($P < 0.05$) male excess in incidence (male:female ratio of crude incidence rates = 1.24, of age-adjusted incidence rates = 1.40) was reduced substantially at prevalence (male:female ratio of crude prevalence rates = 1.00, of age-adjusted prevalence rates = 1.30). The overall distribution of patients by age and sex was altered even more. Whereas the actual number of men and women was almost identical among the incidence cases, there were almost 20% more female prevalence cases. Moreover, the proportion of patients who were older women increased greatly, from 15% of total incidence cases to 25% of total prevalence cases; this change came largely at the expense of middle-aged men and women 40–59 yr old, the proportion of whom declined from 36% to 26% of total incidence and prevalence cases, respectively.

The clinical characteristics of the incidence and the prevalence cases also differed (Table 2). There was a slightly greater proportion of patients with insulin-dependent diabetes and of patients on insulin therapy on prevalence day, while the proportion of patients on oral antidiabetic agents was almost twice as great on prevalence day. Compared with the incidence cases, the proportion of patients with fasting blood glucose levels of 200 mg/dl or more was less at prevalence. The median blood glucose level was substantially greater at the time of initial diagnosis, and the proportion of patients with the classical triad of diabetes symptoms was much greater at that time as well. The distribution of relative weights was about the same in both groups; nearly 60% of both incidence and prevalence cases were obese. The proportion of patients with diabetic macrovascular complications was about one-third greater on prevalence day, while the proportion of patients with microvascular disease was fourfold greater. The statistical significance of these differences could not be assessed due to lack of independence, as some individual patients were in both groups.

How did these differences come about? First, women with diabetes mellitus seem to survive somewhat better than men. Based on more than 10,000 p-y of observation and over 500 deaths, the relative survival 15 yr after the initial diagnosis of diabetes was 83.9% of that expected for women of like age and sex and for men was only 72.9% of that expected. Relative survival varied by age at diagnosis as well. After 15 yr, the survival of those less than 30 yr old at the time of

TABLE 1
Incidence of diabetes mellitus among Rochester, Minnesota, residents 1945–69 and prevalence on 1 January 1970

	Incidence 1945–1969				Prevalence 1 January 1970			
	Men		Women		Men		Women	
Age group	N	Rate (10^5)	N	Rate (10^5)	N	Rate (10^5)	N	Rate (10^5)
0–9	9	8.7	7	7.1	3	54.1	1	19.2
10–19	10	15.5	12	14.3	6	134.0	8	159.5
20–29	13	21.8	11	11.7	16	458.8	12	214.6
30–39	38	62.4	27	41.6	22	639.2	21	631.0
40–49	75	159.1	63	113.1	38	1546.6	34	1258.3
50–59	153	408.9	116	239.2	77	3981.4	60	2448.0
60–69	148	558.6	158	419.6	100	7380.1	105	5117.0
70–79	91	636.6	119	506.7	77	9482.8	134	8595.3
80+	30	643.8	55	538.4	29	8123.2	67	7957.2
Subtotal	567	135.6	568	109.7	368	1541.5	442	1537.1
Age-adjusted*		165.1		117.8		1986.1		1524.0

*Directly age-adjusted to the population structure of United States whites in 1970.

TABLE 2
Clinical characteristics at the time of initial diagnosis of diabetes mellitus among Rochester, Minnesota, residents 1945–69 and on prevalence day, 1 January 1970

	Incidence cases	Prevalence cases
Clinical type (%)		
Insulin-dependent	6.6	7.9
Obese non-insulin-dependent	57.5	58.4
Nonobese non-insulin-dependent	33.3	31.5
Secondary diabetes	2.6	2.2
Treatment (%)		
Insulin	20.1	23.5
Oral agents	12.8	24.2
Diet alone	67.1	52.3
Fasting blood glucose		
Median value (mg/dl)	150	116
≤199 mg/dl (%)	69.9	86.0
200–299 mg/dl (%)	22.9	10.6
≥300 mg/dl (%)	7.2	3.4
Classical symptoms		
One or more (%)	29.1	1.5
Relative weight (%)		
<1.0	12.8	12.1
1.0–1.19	28.7	29.6
≥1.2	58.5	58.3
Complications present		
Macrovascular (%)	21.5	30.6
Microvascular (%)	6.3	25.6

TABLE 3
Relative survival (%) after the initial diagnosis of diabetes mellitus 1945–69 among 1135 Rochester, Minnesota, residents according to various clinical characteristics at the time of diagnosis

	Years after diagnosis		
	5	10	15
Symptoms at diagnosis			
Yes	91.8	82.6	74.5
No	91.7	88.7	81.1
Relative weight			
<1.0	82.3	76.3	76.8
1.0–1.19	88.4	88.5	76.7
≥1.2	94.4	86.5	79.4
Initial fasting blood glucose			
≥300 mg/dl	77.5	67.2	63.2
200–299 mg/dl	89.5	81.4	67.9
≤199 mg/dl	90.2	84.5	78.9
Abnormal GTT alone	101.0	102.0	107.0
Initial treatment			
Insulin	86.7	81.3	71.9
Oral agents	86.0	78.5	68.3
Diet	93.7	88.1	81.4
Clinical type			
Insulin-dependent	93.8	91.1	79.7
Nonobese non-insulin-dependent	84.4	82.2	76.6
Obese non-insulin-dependent	94.6	86.4	79.7

initial diagnosis was 97.0% of that expected and was greater than the relative survival of those 30–59 yr old at first diagnosis (77.4%) or those over 60 yr of age at the initial diagnosis of diabetes (70.3%). Comparable data for relative survival by symptomatology, relative weight, initial fasting blood glucose level, choice of initial therapy, and clinical type of diabetes are displayed in Table 3. Survival after 15 yr was less for those with one or more classical symptoms of diabetes at the time of initial diagnosis, for those initially placed on insulin or oral agents, and decreased with progressively higher initial fasting blood glucose levels.

Short-term survival varied substantially by clinical type of diabetes, but survival at 15 yr after initial diagnosis was similar for the major groups (Table 3). There were too few cases of secondary diabetes to assess survival over any extended period after diagnosis. As might be anticipated, survival was also less among individuals with macro- or microvascular complications at diagnosis. At 10 yr after the initial diagnosis of diabetes, patients with macrovascular complications had 55.1%, and patients with microvascular complications 65.0%, of expected survival. Patients without these vascular complications experienced 94.7% of the survival expected for a group of like age and sex. The survival data will be analyzed in greater detail elsewhere.

In addition to variation in survival, there was also differential migration, with a net immigration of elderly women with diabetes into the community during the study period. About 19% (153) of the 810 prevalence cases had been originally diagnosed elsewhere before moving to Rochester. This group was somewhat larger than the 114 incidence cases who had moved away from the community but who were still alive on 1 January 1970. Compared to those who moved away, moreover, those who moved in were more often older women (Figure 1). This helps explain why the median age of the prevalence cases (66 yr) was greater than that of the incidence cases (61 yr), despite the fact that relative survival

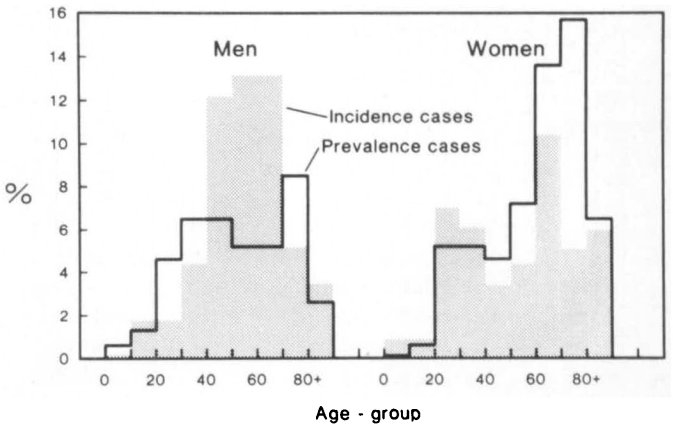

FIG. 1. Distribution by age and sex of 114 original incidence cases who had left the community but were still alive on 1 January 1970 and 153 prevalence cases in Rochester, Minnesota, who had been originally diagnosed elsewhere.

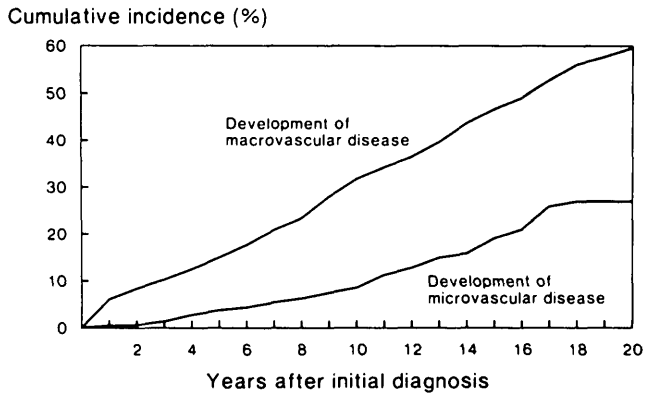

FIG. 2. Actuarially estimated cumulative incidence of macrovascular and microvascular disease after the initial diagnosis of diabetes mellitus among Rochester, Minnesota, residents 1945–69.

was poorest among those over 60 yr old at the time of the initial diagnosis of diabetes mellitus.

A third major factor affecting the characteristics of prevalence relative to incidence cases was the change in the status of individual patients. During the period after diagnosis, the incidence cases were aging, of course; but they were also developing macro- and microvascular complications at a substantial rate (Figure 2). By 20 yr after diagnosis, for example, an actuarially estimated 59.6% of those initially free of macrovascular disease had developed such a complication, while 27.0% of those initially free of microvascular disease had developed retinopathy or diabetic renal disease. Less expected, perhaps, were changes in the clinical nature of the disease, such as those reflected by therapy. Of those initially begun on insulin, 11% of the patients less than 30 yr old and 49% of the patients over age 30 at diagnosis had ceased using insulin. Most of the "decay" occurred during the first year after the diagnosis of diabetes (Figure 3). Conversely, patients who were initially on diet or oral agent therapy were started on insulin subsequently at the rate of over 2% of the group per year, as also shown in Figure 3.

DISCUSSION

There is considerable disagreement from one report to the next on whether diabetes is more common among men or women. Data from the present study show that diabetes could be considered more frequent in men, more frequent in women, and not different from one sex to the other, depending on the indicator used. The incidence of diabetes was greater among men and, if the slightly greater average age of women were taken into account by age-adjusting the rates, this difference was accentuated. If only the numbers of cases by sex were considered, the number of men and women was about equal at the time of initial diagnosis. The crude prevalence rates were essentially equal for men and women, although male prevalence rates were greater after age-adjustment. Among prevalence cases, as clinical series of patients usually are, women outnumbered men. It is apparent that male:female ratios in diabetes research should not be reported without some indication of the manner in which the sex-specific frequencies were determined.

It has generally been agreed that the frequency of diabetes in this country, be it incidence or prevalence, increases with age. Our data show, however, that median age was greater among the prevalence cases. Both the age and sex distributions of prevalence cases were affected by the migration pattern of diabetic individuals. The impact of migration on the prevalence of diabetes mellitus has not been previously assessed to our knowledge. However, the same general phenomenon observed here was also seen for breast cancer, with an influx of older women into Rochester from the surrounding countryside after diagnosis and presumably, in part at least, in response to impaired health status.[7] These data raise the possibility that diabetes prevalence might be somewhat reduced in rural areas near cities, but the prevalence of self-reported diabetes in a national survey was essentially the same (about 20 per 1000) for people living within or outside Standard Metropolitan Statistical Areas; and, outside those areas, it was nearly the same for farm (20.4) and nonfarm residents (20.8).[8]

The clinical spectra of incidence and prevalence cases were also different, in some aspects perhaps less than expected. The distribution of patients by clinical type, for example, was similar for each group. This might have been due to the fact that only modest differences in survival were noted for the different clinical types. The small differences in survival were somewhat surprising, but belief in a more grave prognosis for insulin-dependent diabetes patients may have been influenced by the selective referral to many medical practices of patients who were difficult to manage or who already had poor prognostic signs. In fact, the proportion of patients with insulin-dependent diabetes was somewhat greater on prevalence day than at the time of initial diagnosis. Some of the additional insulin-dependent diabetes on prevalence day may have resulted from changes in the nature of the disease among individual patients. Such changes are implied in the data

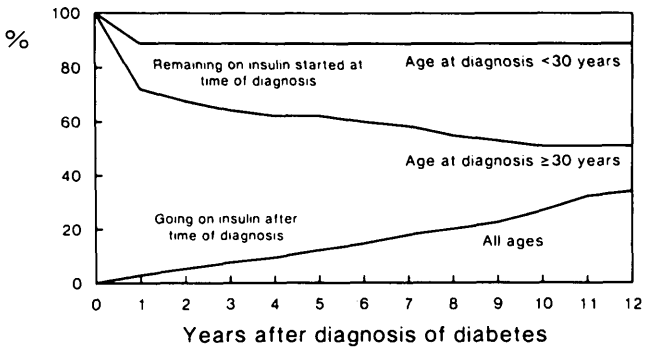

FIG. 3. Actuarially estimated continuance on insulin therapy started at the time of diagnosis by age at diagnosis, and actuarially estimated cumulative incidence of insulin therapy among Rochester, Minnesota, residents originally begun on diet or oral agents.

concerning the proportion of patients newly started on insulin therapy each year. More direct evidence is provided by the observation in this same population of patients that the median time between the onset of "maturity-onset" diabetes and the subsequent first episode of ketoacidosis was 9.1 yr, and one such patient had had diabetes for 35 yr before the initial episode of ketoacidosis.[9]

The proportion of patients who had one or more of the classical triad of diabetes symptoms was much less among the prevalence patients. This was due in part, perhaps, to the less favorable survival among patients with symptoms but is more readily explained by the likelihood that patients were under sufficient control to at least prevent florid symptoms. This was reflected in the lower median fasting blood glucose value for prevalence patients and the lower proportion of that group who had blood glucose levels above 200 mg/dl near prevalence day.

Survival was marginally less among those on oral agents but a greater proportion were so treated on prevalence day. We believe that this is largely due to changing therapeutic fashion. Some patients who were initially started on insulin during the early years of the study did not seem to be insulin dependent in the sense of showing any evidence of being ketosis prone. Many of these patients were later switched to oral agents as these became available and were popularized.

Patients were more likely to have macrovascular than microvascular complications at the time of initial diagnosis, but both were relatively common among the prevalence cases. Even though survival among patients with macrovascular disease was relatively poor, they were replaced at a greater rate by patients developing such complications after diagnosis. Consequently, the proportion of prevalence cases with macrovascular complications was somewhat greater than at initial diagnosis. Patients developed microvascular disease at a lower rate, but the survival experience of those with microvascular disease up to 10 yr after the initial diagnosis was somewhat better as well. Consequently, a quarter of the patients had microvascular disease on prevalence day compared with less than 10% at the time of initial diagnosis.

We conclude that the clinical spectrum of diabetes at the time of initial diagnosis is inherently different from that among surviving prevalence cases at some later time. Such differences should be taken into account when comparing results from studies that involve these two different kinds of diabetic patients.

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