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Mortality in diabetes mellitus—data from a developing region of the world

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Abstract

This retrospective study presents the mortality trends in diabetic patients in a developing region of the world. The data were collected by screening the hospital records of all diabetic patients who died over a period of a decade at Institute of Medical Sciences, a tertiary care medical centre in Kashmir Valley of India. Of 133374 patients admitted to the centre from January 1987 to December 1996, 9627 died, of whom 269 (151 males and 118 females) were recorded to have diabetes mellitus. The mean $\pm$ S.D. age at the time of death was 51.61 $\pm$ 13.77 years for males and 51.50 $\pm$ 15.50 years for females. The common causes contributing to death were infections (33.83%), chronic renal failure (30.85%), coronary artery disease (16.36%), cerebrovascular disease (13.75%), hypoglycaemia (7.81%), diabetic ketoacidosis (6.69%) and hyperosmolar coma (2.23%). In 7.43% patients the cause of death could not be ascertained. Death was attributed to single cause in 60.22%, to two causes in 26.39% and to three or more causes in 5.95%. Most (59.11%) of these diabetic patients died within a week of hospitalisation. We conclude that mortality trends in diabetes mellitus differ in developing regions as compared to developed regions reflecting poor healthcare in general and diabetic care in particular. Unlike in west, where the major killers in diabetic patients are coronary artery disease and cerebrovascular disease, infections and chronic renal failure continue to be leading causes of death in patients with diabetes mellitus in developing regions like ours.

Keywords: Diabetes mellitus; Morbidity; Mortality

1. Introduction

According to the World Bank, the burden of disease in the developed countries differs from that in the developing countries [1]. In India, communicable diseases affect 50.5% of the popu-

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lation compared to 9.7% in a developed country like the US; on the other hand non communicable diseases predominate in the developed countries [2]. The statistics on the underlying cause of death which are published in many countries provide a very inexpensive source of data and allow important trends and changes in the causes of death (and, by extrapolation, the morbidity of various diseases) to be followed both within and between countries. However, the reliability of these statistics has been questioned [3].

Diabetes mellitus is a common clinical disorder causing significant morbidity and mortality. It is not easy to secure data on the causes of death in diabetic patients because of the heterogeneity of diabetes, possible misclassification of the disease, and poor accounting of diabetes on death certificates. The studies on mortality in people with diabetes mellitus in western countries and Japan show that cardiovascular and cerebrovascular diseases are the leading causes of death [4]. The World Health Organisation multinational study of vascular diseases in diabetic patients (age 35–54 years, data compiled from ten countries over 10 years) indicates that compared to the Europeans, the mortality rates were lower for the Asian people with diabetes e.g. age adjusted Europe vs. Asia 10.4 vs. 7.1 per 1000 population [5].

The study of mortality in diabetes is beset with many difficulties. Both long term and short term studies by many authors are available in literature. Most epidemiological data are from countries with more advantaged healthcare and disease surveillance systems. Well collected and statistically evaluated data from our country are scant. In this study we evaluated the pattern of the causes of death in diabetic subjects, using both underlying and contributory causes of death, in a tertiary care centre in Kashmir Valley (India). The data are based on hospital deaths and not on deaths in the community.

2. Materials and methods

The data for this study were obtained from the records division of the Institute of Medical Sciences, Soura, Srinagar, Kashmir, India—a 650 bedded tertiary care medical centre with most of the modern medical facilities. In India, we have healthcare system at three levels, viz. primary care level, secondary care level and tertiary care level. In the Indian context, primary healthcare is provided by the complex of 'Primary Health Centres' through multipurpose workers and village health guides. Secondary level care is provided in district hospitals and community health centres which serve as the first referral level. The tertiary level, a more specialised level, is provided by regional and central level institutions. The data of one decade (1987–1996) were analysed for the total admissions to and total deaths in this centre. One assumes that some deaths occur at secondary care level or in the community unattended, therefore, the data may represent an underestimation of the causes of death. Total number of deaths in diabetic patients during the study period was estimated using the actual number of deaths registered where diabetes was the underlying or a contributory cause. All the death certificates mentioning diabetes as underlying or contributory factor were retrieved. After confirmation of the death, the resident in charge fills in the death certificate which is subsequently scrutinised by one of the faculty members of the concerned department. All the deaths are reviewed regularly by the 'mortality review committee' to authenticate the data. The data were analysed for patient's age, sex, type of diabetes, department to which patient was admitted prior to death, duration of hospital stay prior to death, any complication of diabetes mentioned on the death certificate and any concurrent sickness. Particular attention was paid to the mention of infection and the type of infection, renal failure, cardiovascular disease, cerebrovascular disease, diabetic ketoacidosis, hypoglycaemia, and hyperosmolar non ketotic coma. The comparative analysis of the data obtained was performed by sex, the type of diabetes, the age of the diabetic patient, one or more causes contributing to demise, and duration of the hospital stay prior to death.

2.1. Statistical analysis

The SPSS package (Statistical Programme for the Social Sciences, version 6.0, PC windows) was used for data analysis. In addition to descriptive statistics, the Chi-square test was used to assess the association between categorical variables and the t-test for comparison among continuous variables. Two-tailed P values were calculated and $P < 0.05$ was taken as statistically significant.

3. Results

During one decade from January 1987 to December 1996, 133374 patients were admitted to the Institute of Medical Sciences, Srinagar, Kashmir. In this period 9627 (7.22%) died of whom 269 (2.79%) were recorded to have diabetes mellitus. These 269 diabetic deaths constitute the basic material for this study. Fig. 1 depicts the age and sex distribution of these patients. Mean age of the patients was 51.61 ± 13.77 years in males and 51.50 ± 15.50 years in females. Table 1 shows the age and sex distribution in relation to the type of diabetes. Understandably patients with non-insulin dependent diabetes mellitus (NIDDM) were older than patients with insulin dependent diabetes mellitus (IDDM). Females with IDDM died earlier than their male counterparts though the difference was not statistically significant. Out of these 269 patients 106 (39.40%) were admitted in the Endocrine unit while 163 (60.59%) were admitted to other services like Nephrology (55, 20.45%), Internal Medicine (32, 11.89%), Neurology (24, 8.92%), Cardiology (21, 7.81%), Gastroenterology (13, 4.83%) and other departments (18, 6.69%).

Table 2 gives the details of disorders to which death was attributed in these diabetic patients. The leading causes of death were infections in 91 (33.83%), chronic renal failure in 83 (30.85%), coronary artery disease in 44 (16.36%), cerebrovascular disease in 37 (13.75%), hypoglycaemia in 21 (7.81%), and diabetic ketoacidosis in 18 (6.69%). Other causes to which death was attributed in this study were acute renal failure in 15 (5.58%), malignancy in 12 (4.46%), hyperosmolar coma and chronic liver disease each in six (2.23%), gastrointestinal bleeding in five (1.86%), adult respiratory distress syndrome in four (1.49%), pulmonary thromboembolism in three (1.11%) and rheumatic heart disease, paroxysmal atrial tachycardia, disseminated intravascular coagulation, and acute hepatic failure each in one (0.37%) patient. In 20 (7.43%) the records were

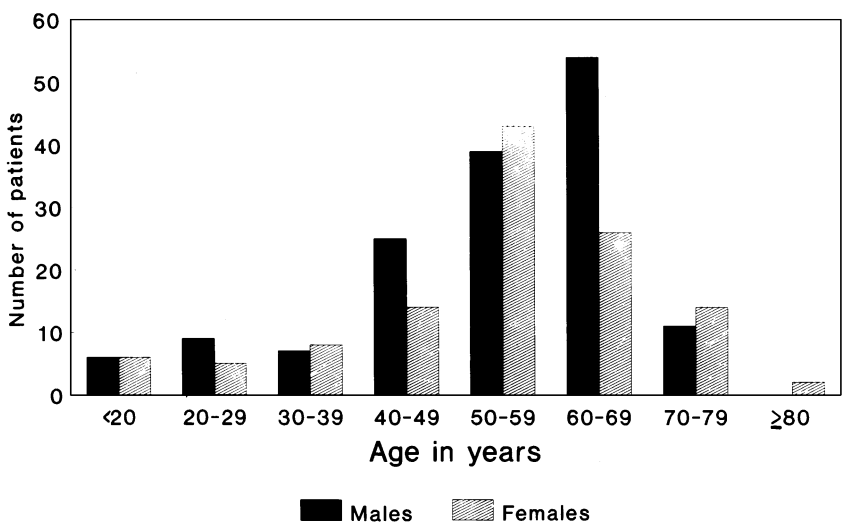

Fig. 1. Frequency of 269 patients in various age groups in relation to sex.

Table 1
Age and sex distribution of 269 patients in relation to type of diabetes

Age group (years)	IDDM*			NIDDM**		
	Males	Females	Total	Males	Females	Total
<30	14	10	24	1	1	2
30–39	5	4	9	2	4	6
40–49	7	2	9	18	12	30
50–59	3	1	4	36	42	78
≥60	—	—	—	65	42	107
All groups	29	17	46	122	101	223

* $\chi^2 = 1.65$, d.f. = 3, $P > 0.6$.
** $\chi^2 = 5.34$, d.f. = 4, $P > 0.2$.

not clear about the cause of death. Table 3 gives the details of patients with one, two, and three or more causes of death. In most patients death was attributed to a single cause. Infection in combination with other causes was the most frequently encountered cause of mortality in our diabetic population. However, as a single cause, chronic renal failure was the most important killer. The various infections encountered included septicaemia in 37 (40.66%), pneumonia in 26 (28.57%), urinary tract infection, and pulmonary tuberculosis each in four (4.40%) and other infections in 20 (21.98%).

A significant number (29.7%) of diabetic deaths in our setting occurred in young (≤ 39 years) or early middle life (40–49 years) patients. Common causes of death in the young included infections (47.22%), diabetic ketoacidosis (13.89%) and hypoglycaemia (13.89%). The single most frequent cause of death in patients in the age group of 40–49 years was chronic renal failure (42.86%).

Analysis of the data for the major causes of mortality revealed no significant age difference between males and females in infections, chronic renal failure, coronary artery disease, or cerebrovascular disease. Table 4 gives the details of number and age of patients with major causes of mortality when seen alone or in combination.

Out of 269 patients, 159 (59.11%) died in the first week (105 in first 48 h), 55 (20.45%) in the second week, 20 (7.43%) in the third week and 19 (7.06%) died more than 3 weeks after hospitalisation. In 16 (5.95%) patients the duration of hospital stay before death could not be ascertained from the records.

4. Discussion

Microvascular and macrovascular disease causes considerable mortality and morbidity both among patients with NIDDM and those with IDDM. Life expectancy in diabetic patients is difficult to predict because there are many variables such as type and severity of diabetes, age at onset and life style. Evaluation of data from death certificates is a relatively simple way of determining the mortality trends with a particular disease. Analysis of various series indicate that the presence of diabetes is not recorded in the death certificates in up to 40–50% of instances [6]. The certification of cause of death is a complex process in which there are a number of stages each of which can lead to a diabetic patient not having diabetes recorded on his or her death certificate. Firstly, it depends on whether the patient had been diagnosed as diabetic (which depends on the general health care and screening), secondly on whether the certifying physician knows the clinical history of the deceased, thirdly on his diagnosis and finally on the part that diabetes played in the death. The source of information being death certificates, it is apparent that there is a dichotomy between the underlying and the contributing causes of death [7]. The immediate cause of death is generally selected more frequently

rather than the underlying cause resulting in their being ranked higher than the actual cause of the disease. In spite of the fact that death certificates may under-report the role of diabetes [6,8,9], it continues to be an easily approachable epidemiological tool to understand the mortality trends in diabetes mellitus in different communities. In developing countries of the world where extensive record keeping is unusual, this is the only available source of such information.

The average life span of an Indian male is 60 years whereas that of an Indian female is 61 years [10]. In our study, the average age at death of a diabetic male was 51.61 ± 13.77 years and that of a diabetic female was 51.50 ± 15.50 years. This suggests that the life-span of a diabetic is significantly reduced in our community. The highest number of deaths in our patients was in the age group of 60–69 years in males and 50–59 years in females. In an American study the highest death rate was in the 65–74 years group while in a French study the highest death rate in diabetics was in the age group over 75 years [11,12]. In an Indian study, age of diabetics at the time of death was 55–61 years [13]. Over the period of last one decade the gross death rate in this hospital has been 7.22 per 100 admissions and diabetic deaths constituted 2.79% of all deaths. Data from Indian subcontinent has shown that diabetes forms 2.5% to 10% of all deaths in hospitals [2]. In a western study diabetes accounted for 2% of all deaths [14].

A significant number (15.24%) of our patients were young (≤ 39 years) and understandably most (80.5%) of them had IDDM. For patients with IDDM insulin therapy transformed an otherwise uniformly fatal disease into one of great optimism. Although in the modern era relatively few IDDM patients succumb to acute metabolic consequences of diabetes such as diabetic ketoacidosis and hypoglycaemia, a significant number of these patients continue to suffer major morbidity and premature death particularly in underdeveloped areas.

In our study 91 (33.83%) patients had infections, 83 (30.85%) chronic renal failure, 44 (16.36%) coronary artery disease, 37 (13.75%) cerebrovascular disease, 21 (7.81%) hypoglycaemia, 18 (6.69%) diabetic ketoacidosis, 12

Table 2
Causes of death in 269 diabetics[a]

	Total no. (%)	IDDM no. (%)	NIDDM no. (%)	*P* value
Infections	91(33.83)	16(34.78)	75(33.63)	>0.09
Chronic renal failure	83(30.85)	13(28.26)	70(31.39)	>0.09
Coronary artery disease	44(16.36)	1(2.17)	43(19.28)	<0.01
Cerebrovascular disease	37(13.75)	2(4.35)	35(15.69)	<0.05
Hypoglycaemia	21(7.81)	8(17.39)	13(5.83)	<0.01
Diabetic ketoacidosis	18(6.69)	12(26.09)	6(2.69)	<0.001
Acute renal failure	15(5.58)	0	15(6.73)	—
Malignancy	12(4.46)	1(2.17)	11(4.93)	>0.25
Hyperosmolar coma	6(2.23)	0	6(2.69)	—
Chronic liver disease	6(2.23)	0	6(2.69)	—
Gastrointestinal bleeding	5(1.86)	1(2.17)	4(1.79)	>0.9
Adult respiratory distress syndrome	4(1.49)	1(2.17)	3(1.34)	—
Pulmonary thromboembolism	3(1.11)	0	3(1.34)	—
Rheumatic heart disease	1(0.37)	0	1(0.45)	—
Paroxysmal atrial tachycardia	1(0.37)	0	1(0.45)	—
Disseminated intravascular coagulation	1(0.37)	0	1(0.45)	—
Hepatic coma	1(0.37)	0	1(0.45)	
Undetermined cause	20(7.43)	5(10.87)	15(6.73)	>0.25
All causes	269(100)	46(100)	223(100)	

[a] Includes patients with more than one cause of death.

Table 3
Proportion of patients with one or more than one cause of death

	Total ($n=269$) no. (%)	IDDM ($n=46$) no. (%)	NIDDM ($n=223$) no. (%)	P value
Single cause	162 (60.22)	27 (58.69)	135 (60.54)	>0.7
Two causes	71 (26.39)	13 (28.26)	58 (26.01)	>0.7
Three or more causes	16 (5.95)	1 (2.17)	15 (6.73)	>0.2
Undetermined cause	20 (7.43)	5 (10.87)	15 (6.73)	>0.2

(4.46%) malignancy, six (2.23%) hyperosmolar coma and six (2.23%) chronic liver disease. In one study major causes of death in diabetics were reported to be infections (25.8%) cardiovascular disease (18.5%), cerebrovascular disease (11.3%), uraemia (8.6%) and diabetic ketoacidosis (1.3%) [15]. Another study also revealed a high percentage of diabetic deaths attributed to infections [16]. In a Japanese study infectious deaths were seen to increase in patients with a relatively high age, male gender, previous history of cerebrovascular disease, relatively lower body mass index and higher fasting plasma glucose levels [17].

Chronic renal failure was the most frequent 'single cause' to which death was attributed in our series. A total of 42% of our patients in early middle life (40–49 years) perished because of this complication. This probably reflects the overall poor glycaemic control in our patients. It has been unequivocally shown in the Diabetes Control and Complications Trial (DCCT) study that excellent glycaemic control significantly lowers the incidence of renal disease in IDDM [18]. Mexican–American elders have a greater risk of dying from NIDDM and renal failure than their non-Hispanic white counterparts suggesting that some races may be genetically predisposed to develop renal disease in diabetes [19]. Urinary albumin excretion has been shown to be an important short term predictor of mortality than previously thought [20]. Cigarette smoking has been shown to be related to the development and progression of diabetic nephropathy [21]. Diabetic patients on dialysis have lower survival rates than non-diabetics [22].

In most of the developed countries, cardiovascular and cerebrovascular diseases constitute the most common disorders contributing to diabetic death. In our patient population, these disorders were far less common than infections and chronic renal failure. One study suggested that diabetes increased the ischaemic heart disease death by nine to ten times for women and two to three times for men [23]. In diabetic patients coronary artery disease and cerebrovascular disease have been shown to be the two major causes of death in developed countries [14,24]. In a Japanese study on mortality in diabetics, cardiovascular disease deaths tended to increase in patients with a relatively higher age, male gender, previous ischaemic heart disease and persistent proteinuria [17]. Studies in England and Wales indicate that the diabetic patients are not experiencing the same fall in cardiovascular mortality as that experienced by the general population [25].

Diabetic ketoacidosis is the number one cause of mortality in diabetic children with an overall mortality of 7% [26]. In one series diabetic ketoacidosis caused 1.3% of total diabetic deaths [15]. Hypoglycaemia resulting in death was more often seen in IDDM patients and hyperosmolar coma was seen in NIDDM patients. Hypoglycaemia is thought to be the primary cause or a contributing cause of death in up to 4% of patients with diabetes [27]. Intensive insulin therapy has been shown to be associated with a 2–3-fold increase in severe hypoglycaemia in IDDM subjects [18]. Diabetic hyperosmolar coma has been reported to have a mortality rate as high as 50% in older (> 50 years) patients [26].

The other important causes of mortality in our 269 diabetic patients were malignancy, chronic liver disease and gastrointestinal bleeding. A small number of patients died because of adult respiratory distress syndrome, pulmonary thromboembolism, rheumatic heart disease and disseminated

Table 4
Comparative age of patients with one or more than one cause of death[a]

	Age in years (mean ± S.D.)				*P* value*
	1 cause	2 causes	≥3 causes	Overall	
Infections	49.69 ± 15.85(35)	49.32 ± 17.43(43)	56.42 ± 6.78(13)	50.41 ± 15.74(91)	>0.3
Chronic renal failure	53.25 ± 12.12(55)	54.36 ± 10.69(22)	60.15 ± 5.32(6)	54.05 ± 11.44(83)	>0.3
Coronary artery disease	58.83 ± 9.26(23)	58.73 ± 10.61(17)	62.50 ± 5.0(4)	59.12 ± 9.42(44)	>0.7
Cerebrovascular disease	54.24 ± 8.55(15)	56.21 ± 13.41(14)	60.11 ± 7.94(8)	56.20 ± 10.48(37)	>0.4
Hypoglycaemia	38.00 ± 20.33(8)	48.91 ± 17.60(11)	50.00 ± 0(2)	44.86 ± 18.16(21)	>0.4
Diabetic ketoacidosis	35.63 ± 20.96(8)	31.14 ± 20.13(7)	53.63 ± 3.18(3)	36.88 ± 19.73(18)	>0.2

[a] Figures in parenthesis indicate number of patients.
* One-way ANOVA.

intravascular coagulation. Apparently these disorders seem to be unrelated to the underlying diabetes mellitus. In a study on major causes of diabetic death, malignancy in 12%, liver disease in 5.4% and gastrointestinal bleeding in 0.7% were among the leading causes of death irrespective of underlying diabetes [15].

This study suggests that infectious disorders and chronic renal failure significantly contribute to mortality in NIDDM as well as IDDM subjects in this community. This is in contradiction with most of the Western literature where the main causes of diabetic mortality are cardiovascular and cerebrovascular diseases. The presence of infections in diabetic population is a reflection of the overall high prevalence of infections in this part of the world [2]. The fact that chronic renal failure was a common cause of mortality in this study suggests poor glycaemic control as a result of economic backwardness, poor understanding of the disease, and non-availability of expert care to most of the diabetic patients.

There is a scope for improving the documentation of data regarding causes of mortality due to diabetes in this part of the world. Further diabetes mortality studies are needed, particularly from developing regions of the world. Well conducted mortality studies can show the relative contribution of diabetes to the total population mortality and they can provide important descriptions of the changes in causes and frequency of diabetes mortality over time. Such an analysis can suggest measures which can reduce unnecessary and early loss of life due to diabetes as well as measures for improvement in long term diabetic care.

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