

Etiological spectrum for mortality in patients with diabetes mellitus at tertiary care hospital in South India

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Abstract

Background: Mortality in diabetes secondary to ketoacidosis or hypoglycemia are rarely reported and underlying co-morbidities are considered as primary cause of death. As diabetes is rarely perceived as a major contributor of mortality in the developing world, this study was undertaken to determine the etiological spectrum of mortality in diabetic patients and to determine associated risk factors. **Methodology:** This is an observational prospective study conducted over two and half years. All diabetic patients above 15 years of age with DM (including newly detected) who succumb to death form the subject for the study. Various risk factors, hematological parameters at the index presentation, co-morbidities and etiology of death were studied in these patients. **Results:** A total of 184 deaths occurred in patients with diabetes mellitus over this study period, in which 116 were male & 68 were females. The mean age at death among these patients was 58.71 in men & 55.76 in women. The leading primary causes of death were Infections (26.4%), Chronic kidney disease [CKD](24%), Cerebrovascular accident [CVA](23.1%), Ischemic heart disease [IHD] (21.5%), Chronic liver disease (3.3%), Chronic obstructive pulmonary disease [COPD] (0.8%) and Diabetic ketoacidosis [DKA] (0.8%). The main contributory cause of death was Infections (46.7%), CKD (22.3%), CVA (20.6%) and IHD. Urosepsis, cellulitis and pneumonia formed the major cause of infections and ARF. **Conclusion:** Infections and chronic renal failure significantly contributed to mortality in diabetic patients in this community. Burden of diabetes in community can be easily understood by studying the mortality trends in the community.

Keywords: diabetes mellitus, mortality, hospital stay, infection.

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Introduction

India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the “diabetes capital of the world”. International diabetes Federation (IDF) estimates that India alone has 61.3 million people living with diabetes; this places India second to China and this number is expected to increase to 69.9 million by the year 2025[1]. The excess global mortality attributable to diabetes mellitus (DM) in the year 2000 was estimated to be 2.9 million, equivalent to 5.2% of all deaths[2]. Most often death occurs due to cardiovascular and renal disease and not from a cause uniquely related to diabetes, such as ketoacidosis or hypoglycemia[3]. The bulk of excess risk of mortality among patients with DM in Western countries has been attributed to circulatory diseases[4]. The scenario is different in Asian and other developing regions of the world where infection and renal failure are more common causes of death among people with diabetes. Also the routine mortality statistics

are based solely on the “underlying cause of death”. Information on mortality and cause of death due to diabetes in India is mainly from retrospective hospital-based clinical or autopsy studies. Under reporting of diabetes as an underlying cause of death on death certificates is very common. Although figures obtained from death certificates have limited use in research or health planning, they do provide comprehensive data, making them useful for studying long-term trends[5]. Evaluation of data from death certificates is a relatively simple way of determining burden of disease and underlying etiologies for mortality. Thus, although it is a great challenge, there is an obvious need to study mortality, its causes and trends among people with diabetes, as diabetes is rarely perceived as a major contributor to mortality in the developing world. This study aimed at providing a more realistic estimate of the number of deaths attributable to diabetes and cause specific mortality among them. This study was undertaken to determine the etiological spectrum of mortality in patients admitted at VIMS Hospital, Bellary & also to determine associated risk factors in them pertaining to hematological abnormalities at the time of hospitalization.

Materials & methods

This is an observational prospective study conducted from January 2013 to June 2015. All diabetic patients above 15 years of age with DM (including newly detected) who succumbed to death as inpatients

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in various departments of VIMS combined hospital, Bellary form the subject for the study. Diabetic Patients less than 15 years and patients who die of unnatural causes (accidents, homicide, etc) are excluded from study group. All the diabetic patients were followed up from the day of admission till death and death certificates mentioning diabetes as underlying or contributory factor were thoroughly studied. The data were analyzed for patient's age, gender, type of diabetes, duration of hospital stay prior to death, any complication of diabetes mentioned on the death certificate and any concurrent sickness. All the hematological parameters and radiological investigations performed relevant to disease during admission were also noted. The causes of death among diabetics were classified into primary and contributory. The contributory cause refers to the etiology mentioned on the death certificate of any cause/disease other than diabetes. When there was mention of only one contributory cause other than diabetes, it was referred to as a primary cause.

Statistics

The data were analyzed descriptively using means, standard deviations and percentages. Tests of significance were performed using independent student t tests and chi-square analyses as appropriate for the variables used in the comparison. The level of significance was set at 0.05. All analysis were performed with the statistical package for the social sciences for windows version 16; SPSS, Chicago.

Results

Table 1: Comparison of various parameters in relation to causes of death in diabetic patients

Causes	Age (Yrs)	Proportion on overall mortality
Infections	54.44	26.4%
CKD	58.24	24%
CVA	60.88	23.1%
IHD	60.89	21.5%
CLD	54.75	3.3%
COPD	55.00	0.8%
DKA	32.00	0.8%
Mean value±SD	54.12±8.7	
P value	0.134	

*CKD- Chronic Kidney disease, COPD- Chronic obstructive pulmonary disease, CVA- Cerebrovascular disease, DKA- Diabetic ketoacidosis, IHD- Ischemic heart disease, CLD- Chronic liver disease, DM- Diabetes Mellitus, SD- Standard deviation.

Among patients with diabetes, Urosepsis (34.3%) were the most common infective cause of death, followed by diabetic foot (21.8%), pneumonia (18.8%), meningococcal meningitis (12.5%), pancreatitis (6.2%), TB (6.2%) and mucormycosis (4%). Urosepsis (36.1%) was the most common cause of ARF, followed by cellulitis (27.7%), pneumonia (22.2%), pancreatitis (5.5%), CVA (2.7%), DKA (2.7%) and meningococcal meningitis (2.7%).

The mean duration of diabetes was 5.4 years and it was significantly lower in DKA, chronic obstructive pulmonary disease and infections in the range of 3, 4 and 4.5 years respectively (table 2).

Table 2: Comparison of various causes of death with duration of diabetes and hospital stay

Causes	Hospital stay (hrs)	Duration of DM (yrs)
CKD	108.276	7.690
COPD	200.000	4.000
CVA	51.673	5.385
DKA	24.000	3.000
IHD	34.321	5.304
Infections	69.031	4.516
CLD	73.000	8.000
Mean value±SD	78.93±51.8	5.410±1.6
P value	0.001	0.06

The mean period of hospital stay was 71.4 hours. This was less than 2 days in IHD and DKA. The mean period of hospital stay among infective and non-infective causes (in hours) was 69.03 and 80.39 (p<0.05) respectively.

Among this study group, 6 were newly detected diabetics and all 6 had infection as a contributory cause. In the deaths due to IHD, 6 (21.4%) were due to acute myocardial Infarction. Patients with CVA, CKD and IHD had a significant history of hypertension. The hematological abnormalities at the time of hospitalisation in these patients are depicted in table 3.

Table 3: Comparison of hematological parameters among various etiologies for mortality in patients with DM in the study

Causes	RBS (mg/dl)	HB(gm/dl)	WBC count(cells/cu.m)	UREA (mg/dl)	CREATININE(mg/dl)	SODIUM (mEq/l)
CKD	137.52	10.120000	11175.08	122.36	5.900000	130.79
COPD	103.00	10.800000	12400.00	55.00	.800000	134.00
CVA	180.44	11.025000	10926.20	39.38	1.113636	131.04
DKA	410.00	14.000000	26000.00	108.00	1.600000	124.00
IHD	205.00	10.516667	11138.22	38.23	1.181818	135.21
Infection	242.59	11.018519	11944.29	68.63	2.046875	130.38

CLD	88.50	10.725000	11829.00	64.75	2.175000	127.75
Mean value±SD	200.45±95.7	11.10±1.1	13363.44±4797.8	71.65±28.3	2.22±1.5	130.67±3.0
P value	0.001	0.364	0.238	0.001	0.001	0.108

*CKD- Chronic Kidney disease, COPD- Chronic obstructive pulmonary disease, CVA- Cerebrovascular disease, DKA- Diabetic ketoacidosis, IHD- Ischemic heart disease, CLD- Chronic liver disease, RBS- Random blood sugar, HB- Hemoglobin, WBC- White blood cell.

Mean HbA1c done among 32 patients in the study group was 9.55 (p<0.05). The mean serum RBS (Random Blood Sugar) among all patients was 200.45 mg/dl and was significantly higher in patients with DKA, IHD and infections. Mean serum creatinine (mg/dl) in causes other than renal diseases was 2.69. RBS, serum urea and creatinine were significantly higher in various disease as compared to mean values. CKD (130.79mEq/l), DKA(124mEq/l), Infections (130.38 mEq/l) and Liver diseases (127.75mEq/l) had low sodium levels.

Discussion

This is a hospital-based study of mortality pattern in patients with diabetes from north Karnataka and shows that the infections and renal disease contribute to most deaths of people with diabetes in this part of the world. As life expectancy in patients with diabetes is difficult to predict because of many confounding variables such as type and severity of diabetes, age at onset, associated co morbidities due to diabetes & regularity in undergoing treatment, we believe that evaluation of data from death certificates is a relatively simple way of determining the mortality pattern. Diabetes constituted 4.23% of total deaths of hospital in this period and this figure were almost double the figures reported in other parts of India, which is 2.7% from Northern part of India and 2.8% from Kashmir[6,7]. In our study, we found that mean age of death in hospital (58.71 years in men and 55.76 years in women with diabetes) was significantly lower than the average life expectancy (63.9 years in men; 66.9 years in women) in India as per 2001 census[8]. This is comparable with the study conducted by Zargar et al in Kashmir, in which mean age (SD) of death was 58.76 (13.58) and 57.4 (13.4) years, respectively[7]. An Indian study by Das et al reported the age at the time of death for people with diabetes to be 55–61 years. In this study, which was carried out over 1 year, it was observed that mortality among hospitalised patients with non-insulin-dependent DM was nearly 20%[9]. One can argue that our study, as well as that of Zargar et al and Das et al is hospital based, and hence the findings cannot be extrapolated to a community where many deaths occur unattended. In a population-based study from south India by Mohan et al reported the mean age of death among people with diabetes to be 66 years[13]. However, population-based studies have drawbacks like unavailable evidence of the cause of death, inaccuracy of verbal accounts, and non-availability of medical records. In our study, infections constituted the major cause of death, both as primary and contributory cause. This high ratio is comparable with two studies done in Kashmir in the past few decades[7,10]. However, more recent studies from developed and some developing countries found that a much smaller proportion of death certificates for people with diabetes mentioned infectious disease[11,12]. As ours is a hospital-based study, the prevalence of infection may have been higher. Nonetheless, low literacy rates and poor public health infrastructure, and ignorance with strict diabetic control, socio-economic factors may all be contributory factors for such numbers[13]. Our study is also comparable with Sasisekhar et al in which Infections was the major cause of death constituting 30.1%[14]. The presence of infections in diabetic population is a reflection of the overall high prevalence of infections in this part of the world. Poor education about complications of infections, late presentation to hospital, inappropriate use of antibiotics and delay in treatment of sepsis are some of reasons for such high mortality in diabetic patients. Chronic kidney disease was the second most common cause of death in our study. This reflects the generally poor glucose and hypertension control in these patients with diabetes. In the population-based study by Mohan et al, the second most common cause of death in patients with diabetes was renal disease, accounting

for 23.5% of deaths[13]. Even in the study done by Zargar et al, renal diseases constituted second common cause accounting for 33.6%[7]. About 16 million people in the United States have diabetes, and about 100,000 people have kidney failure as a result of diabetes[15]. Acute renal failure constituted major contributory factor in these patients. Urosepsis (27.8%) was the most common cause of ARF, followed by Cellulitis (27.2%) and pneumonia (22.2%). Circulatory disorders including IHD and CVA constituted next common causes. In a study conducted by Zargar et al by studying hospital records retrospectively showed 16.9% and 13.2% of deaths due to IHD and CVA[7]. Our study is also comparable with the study done by Bhansali et al, which was a retrospective study in which 17.4% deaths were due to IHD[6]. However, studies in Kerala shows cardiovascular cause as major cause followed by infections. In the study by Jimmy Antony et al, circulatory causes were most common accounting 21.73% of IHD and 5.31% of CVA deaths[16]. American Diabetes Association revealed that cardio vascular diseases are the leading causes of morbidity and mortality in diabetic patients[17]. Higher mortality rates have been reported in Western Australia 63% and also in UK 71%[18,19,20]. It is well known that the rate of reporting of diabetes on CVD (Cardiovascular disease) death certificates remains poor[21]. Reasons for the lower contribution of CVD to diabetic mortality in our study may be the demise of some young patients from infections before they could die from CVD, and, also because many CVD-related deaths may occur before patients make it to the hospital because of higher chances of sudden death. Liver diseases and COPD constituted 3.3% and 2.7% of total deaths in our study respectively. This is comparable with the study done in Kashmir, in which it was 2.7%[7]. Sasisekhar et al showed a lower rate of 0.7% deaths due to COPD[14]. Complications related to DKA accounted for 0.8% of deaths. In Kerala study, deaths attributable to diabetes mellitus as an underlying cause of death in 17 cases (8.21%) which includes hypoglycemia 2 (0.97%), hyperglycemia 1 (0.48%) and DKA 14 (6.76%)[16]. DKA causes up to a third of all deaths in people with diabetes younger than 24 years [22]. With appropriate therapy, the mortality rate of DKA is low (<5%) and is related to underlying or precipitating event such as infections or myocardial infarction. This study also mentions the hematological abnormalities at the time of hospitalization. Mean RBS (Random Blood Sugar) was significantly higher in patients with IHD and infections. Hyperglycemia not only precipitates many infections, it is also an independent risk factor for IHD, CKD and CVA. In our study, mean serum creatinine of >2 mg/dl was found in patients with infections, liver diseases and with multiple causes of death apart from patients with CKD. This signifies the impairment in kidney, even before presenting to a tertiary centre and hence having a high mortality.

Conclusion

India experience an epidemic of diabetes and routine mortality statistics based on underlying cause of death underestimate the seriousness of the problem. Life expectancy in diabetic patients is difficult to predict because there are many variables such as type and severity of diabetes, age at onset, associated co morbidities due to diabetes & regularity in undergoing treatment. However, the burden of diabetes in community can be easily understood by studying the mortality trends in the community. This study suggests that infections and chronic renal failure significantly contributed to mortality in diabetic patients in this community. This is in contradiction with most of the Western literature. The average life expectancy of diabetic patients is significantly reduced in diabetic patients. Although males are most commonly involved, life expectancy is markedly reduced in females. The mean duration of diabetes before death was significantly lower in DKA, chronic obstructive pulmonary disease and Infections. Reducing the risk of infection by strict glycemic control, early referral, and creating awareness about preventive strategies for complications of diabetes will help in reducing mortality in our patients.

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