INTRODUCTION

Diabetes mellitus (DM) is the leading cause of morbidity and mortality in India [1,2]. A recent national survey of diabetes conducted in six major cities in India: New Delhi, Chennai, Bangalore, Hyderabad, Kolkata, and Mumbai gave a prevalence of diabetes and impaired glucose tolerance in urban adults of 12.1% and 14.0%, respectively [1]. According to the World Health Organization estimates, India had nearly 19.4 million adults with diabetes in 1995 and is projected to have 72.2 million by 2025 [3]. Of the estimated 25 million persons with diabetes in India in 1999, only 3.6 million received pharmacological treatment [4]. The Bangladesh Urban Diabetes Study estimated that the annual direct cost for diabetes care in 1998 was about US$ 191, and the mean direct cost per hospitalization for a diabetes-related event was about US$ 208 [5]. The per capita expenditure on health care in India is only 6.4% of the average world spending on health, while India accounts for 23.5% of the world's disability-adjusted life years lost due to diabetes [6]. Epidemiologic studies on mortality in DM in the Western countries and Japan showed that cardiovascular and cerebrovascular diseases are the leading causes of death [7-14], while no such information is available from India and other developing countries. A few earlier hospital based studies from India had reported infection and chronic renal failure as the leading causes of death in hospitalized patients [15,16]. Due to scant information on mortality in diabetes from this part of the world where the prevalence of diabetes and its related complications is still increasing, this study was undertaken with these objectives:

1. To assess the mortality pattern of diabetes mellitus
2. To analyze the cause of death in diabetes mellitus
3. To compare the mortality pattern of diabetes mellitus with nondiabetes patients

METHODS

In this retrospective study, all the information was collected from inpatients' medical records at IMS and SUM Hospital, Bhubaneswar, India, from January 2012 to December 2015 and rerecorded in a structured format. This study is approved from our Institutional Ethics Committee. SUM Hospital is a large multidisciplinary teaching hospital in Eastern India with over 1 million outpatients and 1,65,388 were admitted during the study period. All death case files (1590) were retrieved. Each file was scrutinized for confirmation of the diagnosis of DM and its reason(s) for admission and secondary/tertiary disease or diabetes related complications contributing to death [17]. Data collected were age, sex, blood glucose at presentation, evidence of micro- and macrovascular complications, concurrent illness and time in hospital preceding death. Cause of death was evaluated with respect to (1) presence of diabetes-related complications and (2) associated illnesses. Some patients died of diseases unrelated to diabetes such as malignancy (other than carcinoma pancreas), gastrointestinal bleeding, and hepatic failure/cirrhosis. These were classified as diabetes unrelated deaths. The cause of death (single or multiple) was compared with nondiabetic patients died during this period.

Statistical analysis

The Statistical Program for the Social Sciences, version 7.5, PC Windows package was used for data analysis. In addition to descriptive statistics, the χ²-test was used to assess the association between categorical variables and t-test for comparison among continuous variables. Two-tailed p-values were calculated, and PB/0.05 was taken as statistically significant.

RESULT

In this 4-year retrospective study, it was revealed that 1590 adult patients died in this hospital out of total 1,65,388 adult admissions.
Out of 1590 deaths, 442 patients had diabetes and rest did not have diabetes. A t-test was analyzed between the patients died with diabetes and without diabetes and found not significant as it is equally distributed in both groups (p=0.9, Table 1). It was observed that the death of patients in both diabetes and nondiabetes groups were on increasing order according to increasing age (Fig. 1).

All patients died with diabetes were classified it into two groups, i.e., with diabetes-related disease (DRD) (377 patients) and diabetes non-related diseases (DNRD) (65 patients). From t-test, it was revealed that it is highly significant (p=0.02). Hence, the patients with diabetes have much higher chance of death if they have DRD compared to those with DNRD in the same age groups (Table 2). The diabetes patients with diabetes complications had much higher chance of death compared to those with non DRD in all the age group (Fig. 2).

We also tried to check for any significant difference in sex for NDM as far as mortality for a particular complication is concerned. However, we found all the complications leading to death were equally distributed in both sexes except infection. In the case of infection, M: F was 117:53 which was statistically significant at p=0.03 (Table 3).

Our study revealed that the diabetes patients with more complications had more chance of death compared to those having less complications. We had 17.87% deaths with one complication, 35.29% deaths with two complications and 46.83% with three or more complications. The hospital stay before death also diminishes as the number of complications increased (Table 4).

There were 1148 deaths without diabetes, with a mean age at death 66.4 years (M:F - 67.5:65.3). Contributory factors were infections - 34.39% (average age 69.2 years), stroke - 1.66% (average age 68.7 years), CKD - 1.92% (average age 61.2 years), coronary artery disease (CAD) - 1.57% (average age 68.1 years), heart Failure - 1.83% (average age 71.2 years). Death due to other diseases such as malignancy, seizures, burns, and accidents were 31.71%. The diabetes patients died in less hospital stay period than nondiabetes patients, it was statistically significant as p=0.009 (Table 5).

In those having DM, contributory factors for death were infections - 39.37% (M-63%, F-37%) average age 59.8 years, CKD - 18.55% (M-76%, F-24%) average age 63.9 years, CAD - 14.7% (M-66%, F-34%) average age 63.58 years, stroke - 1.35% (M-70%, F-30%) average age was 65.3 years, heart failure - 7.24% (M-76%, F-24%).

Table 1: Death of patients with or without diabetes according to age group

| Age group | DM (N=442) | NDM (N=1148) |
|-----------|------------|--------------|
|           | Male | Female | Total (%) | Male | Female | Total (%) |
| 15-24     | 9    | 7      | 16 (3.62)  | 36   | 25     | 61 (5.31) |
| 25-34     | 16   | 5      | 21 (4.75)  | 64   | 46     | 110 (9.58) |
| 35-44     | 25   | 2      | 27 (6.11)  | 72   | 58     | 130 (11.32) |
| 45-54     | 53   | 36     | 89 (20.14) | 96   | 79     | 175 (15.24) |
| >65       | 110  | 49     | 159 (35.97) | 263  | 134    | 397 (34.58) |
| Total     | 294  | 148    | 442 (100.00) | 712  | 436    | 1148 (100.00) |

DM: Diabetes mellitus, NDM: Nondiabetes mellitus

Table 2: Death with diabetes (N=442)

| Age group | DRD | DNRD |
|-----------|-----|------|
|           | Male | Female | Total (%) | Male | Female | Total (%) |
| 15-24     | 7    | 5      | 12 (2.71)  | 1    | 2      | 3 (0.68)  |
| 25-34     | 5    | 4      | 9 (2.04)   | 2    | 2      | 4 (0.90)  |
| 35-44     | 32   | 15     | 47 (10.63) | 6    | 3      | 9 (2.04)  |
| 45-54     | 56   | 29     | 85 (19.23) | 5    | 4      | 9 (2.04)  |
| 55-64     | 71   | 30     | 101 (22.85)| 6    | 5      | 9 (2.04)  |
| >65       | 83   | 40     | 123 (27.83)| 22   | 7      | 29 (5.56) |
| Total     | 254  | 123    | 377 (85.29)| 42   | 23     | 65 (14.71) |

DRD: Diabetes related diseases, DNRD: Diabetes non-related diseases

Table 3: Death without diabetics (N=1148)

| Disease   | Sex | Number of death | Average age at death | p value |
|-----------|-----|----------------|----------------------|--------|
| CKD       | M   | 62             | 62.81±13.22           | 0.29   |
|           | F   | 20             | 62.1255±14.28         |        |
| CAD       | M   | 42             | 64.38±14.17           | 0.78   |
|           | F   | 23             | 63.23±14.15           |        |
| CVA       | M   | 36             | 63.73±10.21           | 0.66   |
|           | F   | 24             | 62.52±12.83           |        |
| CHF       | M   | 18             | 68.03±15.5            | 0.56   |
|           | F   | 14             | 66.39±17.6            |        |
| Infection | M   | 117            | 61.92±12.24           | 0.03   |
|           | F   | 53             | 61.23±13.45           |        |

Table 4: Duration of hospital stay in diabetics with number of complication

| Complication | Number of death (%) | Hospital stay in days |
|--------------|---------------------|-----------------------|
| One complication | 79 (17.87) | 25 |
| Two complication | 156 (35.29) | 9 |
| Three or more complication | 207 (46.83) | 4 |
| Total | 442 (100) | - |
F-2.4%) average age 67.31 years, deaths not related to diabetes were 14.7%. The percentage of overall deaths due to leading causes in diabetes and non-diabetes was compared with t-test and it was revealed highly significant (p=0.01, Table 5).

The death of DM due to CVA was classified into two groups, ischemic and hemorrhagic with respect to age group. It was revealed with t-test, i.e. there was no any significant between groups (p=0.10). Whereas in total, irrespective of the age, with \( \chi^2 \) it was revealed that death due to hemorrhage was more as compared to ischemic (p=0.00001, Table 6).

**DISCUSSION**

Mortality in diabetes is influenced by long-term vascular complications of diabetes, uncontrolled hyperglycemia; its metabolic sequelae, and/or treatment induced hypoglycemia. In most countries, mortality records under report diabetes as the primary, or underlying/contributory disease causing death [9,18-21]. Analyses of US death certificates (1999) indicate that the presence of diabetes is recorded in only 40-50% and is represented as a contributory cause of death in only 10-15% patients [22]. Factors contributing to increased mortality trends in developing countries include lack of awareness, poor drug compliance, inadequate secondary/tertiary hospital care facilities, unorganized referral system, poor patient transport service, affordability, and availability of effective drugs. Our study is an important addition to the scant literature in the mortality statistics of Indians with diabetes. Earlier data from other centers in India have shown that diabetes accounts for 2.5-10% of all deaths in hospital [15,23,24]. This is much higher with our observation of a 27.8% overall death rate in diabetes patients. It is higher as compared to other studies of India also. People in the eastern zone of the country have very poor drug compliance and they reach a secondary or tertiary care center only after landing up in complications [25]. Study from Netherlands reported less death with diabetes [26], while that from Canada is still lower [16].

We recorded the highest number of deaths in the age group of >65 years in patients with diabetes. Infection (39.3%) accounted for the largest number of deaths in diabetes in our study. A high prevalence of infection-related mortality has been reported in other studies from India. Zargar et al. from Srinagar, Kashmir Valley reported 33.8% of all deaths related to infection [15]. In another Indian study, Das et al. from Orissa made a similar observation on infection related mortality (33.7%) in diabetes [23]. The infection has also been noted as the leading cause of death in diabetic inpatients from China and Brazil [27,28]. Of the infections, bronchopneumonia with pulmonary tuberculosis accounted for 19% of all diabetes deaths. Most of these patients were chronic bidi/cigarette smokers and had a history of repeated chest infection in preceding years. In Brunei, diabetes (67%) was the most common predisposing factor for melioidosis, a serious pulmonary infection with high mortality [29]. In a population-based mortality study in the US, diabetes conferred 4 times increased mortality risk in the younger age group and almost twice mortality risk in the older age group from pneumonia and influenza [30]. Mortality and morbidity increased significantly among people with diabetes during epidemics of pneumonia and influenza [31,32].

Individuals with diabetes carry a higher risk of severe chest infection through altered defense mechanisms from hyperglycemia, obesity and/or the effect of neuropathy and impaired tissue perfusion [33,34]. Diabetic foot and related sepsis were the second most common form of infection-related mortality. The habit of barefoot walking, working in fields in the country side and poor foot care predispose diabetics to recurrent trauma and infection. Poor socioeconomic status, lack of proper awareness of the disease and delayed presentation could be other important contributory factors. After infection, the second most common DRD was chronic kidney disease (CKD). The incidence rate was 18.55% in our study. CAD was the next common cause of death 14.71% in diabetes. Various clinical and epidemiological investigations from the West provide unequivocal evidence for cardiovascular (60%) and cerebrovascular diseases (15%) as the leading causes of mortality in diabetes [7-13]. Out of 9 patients presenting with DKA in our study, most of them died due to delayed admission and complicating infections. In other Indian studies, deaths from DKA ranged from 6.7 to 20% [14,35]. In a study, it was revealed that uncontrolled diabetes for the first few years can cause acute cardiac and renal complications which are life-threatening [36]. Comparison of blood glucose at presenting and follow-up in association with education and counseling led to betterment of disease, outcome. Most of the diabetic hyperosmolar coma deaths occurred with infection. The death due to CVA in DM was more in hemorrhage as compared to ischemic (p=0.00001). In another study, it was revealed that efforts are needed to increase the medication adherence of these patients so they can realize the full benefits of prescribed therapies [37]. This is an in-hospital study covering only those who died in a hospital. Hence, this does not reflect any scenario in the society at large population. A total of 1587 deaths in 4 years (average yearly adult deaths 397) against approx 42000 admissions per year are to low. This is probably due to very liberal policy of admission, this being a new upcoming hospital.

**CONCLUSION**

There has been an increase in diabetes-related mortality over the past decade. Unlike most of the western studies where CAD and stroke were the leading causes of death in diabetics, in our study, we found infection and CKD to be the leading causes. The overall increased mortality appears also attributable to the prevalence of cardiovascular diseases. Therefore, policy makers should pay more attentions to primary prevention of diabetes to reduce the incidence of death. While placing priority on the prevention of cardiovascular diseases, awareness must also be increased regarding any form of infection which should alarm the patient for medical attention to reduce the burden of diabetes.

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**Table 5: Leading cause of death**

| Disease                  | Diabetics (442) | Non-diabetics (1148) |
|--------------------------|-----------------|----------------------|
|                          | NP % | AHS | NP % | AHS |
| Infection                | 174  | 39.37 | 6 | 395 | 34.11 | 11 |
| CAD                      | 65 | 14.71 | 2 | 18 | 1.57 | 7 |
| CKD                      | 82 | 18.55 | 7 | 22 | 1.92 | 20 |
| CHF                      | 32 | 7.24 | 7 | 21 | 1.83 | 10 |
| CVA                      | 60 | 13.57 | 2 | 19 | 1.66 | 18 |
| DKA                      | 9 | 2.04 | 6 | - | - |
| Hyperosmolar coma        | 5 | 1.13 | 4 | - | - |
| Hypoglycemia             | 4 | 0.90 | 2 | 12 | 1.05 | 19 |
| Diabetic non-related disease |     |     |     |     |     |     |
| Gastrointestinal bleeding | 9 | 2.04 | 14 | 98 | 8.54 | 12 |
| Malignancy               | 5 | 1.13 | 56 | 166 | 14.46 | 27 |
| Others                   | 17 | 3.85 | 23 | 364 | 31.71 | 36 |

**Table 6: Comparison of type of CVA in fatal cases of DM**

| S. No | Age | Ischemic | Hemorrhagic | p value |
|-------|-----|----------|-------------|---------|
| 1     | 40-50 | 2 | 5 | 0.1845 |
| 2     | 51-60 | 6 | 24 | 0.0091 |
| 3     | 61-70 | 7 | 10 | 0.0091 |
| 4     | 71-80 | 5 | 7 | 0.0091 |
| 5     | 81-90 | 2 | 2 | 0.0091 |

NP: Number of patients, AHS: Average hospital stay, CAD: Coronary artery disease, CKD: Chronic kidney disease, CHF: Congestive heart failure, CVA: Cerebrovascular disease, DKA: Diabetic ketoacidosis.
related deaths. It is also important to make the population aware of early screening for diabetes and ensure good glycemic control from the early stage to prevent/delay development of CKD.

ACKNOWLEDGMENTS

Authors are thankful to Prof. (Dr.) Gangadhar Sahoo, Dean, IMS and SUM Hospital, Prof. Manoj Ranjan Nayak, President, Siksha ‘O’ Anusandhan University for extending facilities in this research.

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