Abstract

Objectives: Diabetes is commonly observed to be associated with several comorbidities, out of which cardiovascular comorbidities are most frequently observed. The present study has been done to estimate the proportion of cardiovascular comorbidities among patients of diabetes and to compare it with that of matched nondiabetics. It also aimed to compare the quality of life (QOL) scores and the cost of treatment between diabetics and nondiabetics with cardiovascular comorbidities. Methodology: A hospital-based comparative analytical study was conducted in a tertiary care hospital of Uttarakhand, India. One hundred and ninety-five diabetic were compared with an equal number of age- and gender-matched nondiabetics. We compared the two groups for the presence of comorbidities by Chi-square test and for QOL and cost of care by independent t-test. Regression was done to study factors associated with direct cost incurred for treatment among diabetics with cardiovascular comorbidity. Results: The present study reported about four-time higher risk (odds ratio: 3.9; confidence interval: 2.5–6.1) of comorbidities of cardiovascular system (CVS) among diabetics as compared to nondiabetics. QOL scores were reported to be significantly lower among diabetics with comorbidities of CVS in comparison to nondiabetics. Significant predictors of direct cost among diabetics were religion, marital status, income, and use of alcohol. Conclusion: Cardiovascular comorbidities have been reported to be four times higher among diabetics in comparison to nondiabetics, leading to an adverse effect on QOL and increased expenditure on treatment.

Keywords: Cardiovascular diseases, comorbidity, diabetes, direct cost, quality of life

INTRODUCTION

Diabetes and cardiovascular diseases (CVDs) are two distinct disease groups, which are closely connected due to their common risk factors. Together, they work synergistically leading to increased risk of morbidity and mortality. They also pose a major pressure on our health systems ranging from preventive services to long-term complex care.

A recent systematic review showed that CVDs affect 32.2% of diabetics and is one of the major causes of mortality among them.[1] Studies have shown that the prevalence of various diseases among diabetics range from 2% (Peripheral artery disease [PAD]) to 65% (hypertension).[2] CVDs lead to 31% of all the deaths globally, and the global prevalence of diabetes mellitus is reported to be 8.8%.[3] The situation seems to be more critical in countries such as China, India, USA, Brazil, and Indonesia, where half of the adults with diabetes live. In 2015, approximately 5.0 million people were estimated to have died from diabetes, and majority of these were as a result of cardiovascular complications.[4] It is a common observation that, with the increase in duration of diabetes, quality of life (QOL) decreases while the cost of treatment is expected to increase. Studies comparing QOL scores between diabetics and age- and gender-matched nondiabetics with cardiovascular comorbidities are very
few. Such comparisons would help us quantify the effect of comorbidities on QOL, which is one of the objectives of the study.

In addition to the enormous health and social burden of comorbidities of cardiovascular system (CVS) and diabetes, the direct health-care costs are substantial. India ranked four in total health-care expenditure on diabetes in world. Management of diabetes and its complication can be expensive and is an obstacle in strengthening of health system and achieving Universal Health Coverage in India. However, data on cost incurred in managing diabetes complications are limited. Therefore, one of the objectives of the present study was to assess and compare the direct cost between diabetics with cardiovascular comorbidity to that of nondiabetics with cardiovascular comorbidity.

Despite the clear relationship between diabetes and CVDs, studies assessing various aspects of CVS comorbidities among diabetics are limited in number. Corresponding data from the state of Uttarakhand, a hilly region is unavailable. Therefore, the present study was aimed to assess and compare the proportion of various cardiovascular comorbidities, their QOL and direct cost of treatment among patients of diabetes, and age- and gender-matched nondiabetics with cardiovascular comorbidity.

**METHODOLOGY**

**Study setting**

The present study was conducted in Hemwati Nandan Bahuguna Base Hospital which is a tertiary care hospital of Veer Chandra Singh Garhwal Government Medical Sciences located in Srinagar tehsil of Pauri district in Garhwal division of Uttarakhand, India.

**Study design, sample size, and selection of participants**

The study was a hospital-based comparative analytical study where 195 diabetics (Group 1) were compared with equal number of nondiabetics (Group 2). Group 1 included participants aged equal to or more than 30 years who were under treatment for Type 2 diabetes mellitus for equal to or more than 6 months and were selected consecutively from medicine outpatient department (OPD) of the hospital. The Group 2 included equal number of participants who were age (within 2 years band) and gender matched and were selected among the attendants of patients consulting for acute diseases in different OPDs of the hospital and were unrelated to diabetics. The nondiabetics were also selected consecutively and were those who had no history of diabetes, which was further confirmed by random blood sugar <126 mg/dl by a glucometer. The process was continued till the desired sample size was completed.

**Tools of data collection**

The study was conducted from 2016 to 2019. A pretested quantitative structured questionnaire was used to record information on comorbidities, QOL, and cost of treatment from participants in both the groups.

Four comorbidities such as hypertension, myocardial infarction (MI), coronary artery disease (CAD), and Peripheral artery disease (PAD) were assessed. For obtaining information on these comorbidities, participants were first enquired about the presence of such condition, and based on their responses, the comorbid conditions were cross verified by clinical examination and their medical records. Complete clinical examination of CVS was also carried among all the participants for any hidden/ unreported comorbid conditions. Hypertension and PAD were assessed by measuring blood pressure and Ankle-brachial index, while angina/CAD assessed based on history and medical records.

We used the standard World Health Organization QOL-BREF (WHOQOL-BREF) questionnaire (Hindi version) which is a 26-item specific instrument for measuring QOL and it covers four domains of health which are physical, psychological, social, and environment domain.

In addition, direct cost of treatment for the past 6 months was obtained on consultancy/outpatient ticket fee, outpatient

| Table 1: Background characteristics of the participants (n=195) |
|-------------------------------------------------------------|
| **Characteristic**                                          | **Diabetics, n (%)** | **Nondiabetics, n (%)** |
|-------------------------------------------------------------|
| Age (years), mean±SD                                       | 56.8±12.4            | 56.4±12.3               |
| <40                                                         | 25 (12.8)            | 24 (12.3)               |
| 40-49                                                      | 31 (15.9)            | 32 (16.4)               |
| 50-59                                                      | 51 (26.2)            | 52 (26.7)               |
| ≥60                                                        | 88 (45.1)            | 87 (44.6)               |
| Gender                                                     |                        |                         |
| Male                                                       | 112 (57.4)           | 110 (56.4)              |
| Female                                                     | 83 (42.6)            | 85 (43.6)               |
| Marital status                                             |                        |                         |
| Married                                                    | 163 (83.6)           | 169 (86.7)              |
| Unmarried/divorced/ widowed                                | 32 (16.4)            | 26 (13.3)               |
| Religion                                                   |                        |                         |
| Hindu                                                      | 160 (82.1)           | 162 (83.1)              |
| Muslim                                                     | 30 (15.4)            | 29 (14.9)               |
| Sikh                                                       | 3 (1.5)              | 2 (1.0)                 |
| Other                                                       | 0 (0.0)              | 1 (0.5)                 |
| Socioeconomic status*                                      |                        |                         |
| Upper                                                      | 62 (31.8)            | 39 (20.0)               |
| Upper middle                                               | 102 (52.3)           | 108 (55.4)              |
| Middle class                                               | 29 (14.9)            | 47 (24.1)               |
| Low                                                        | 2 (1.1)              | 1 (0.5)                 |
| Average family size (mean±SD)                              | 5.08±2.6             | 5.23±2.6                |
| Family history of diabetes**                               | 85 (43.6)            | 25 (12.8)               |
| Tobacco use*                                               |                        |                         |
| Current user                                               | 55 (28.2)            | 76 (39.0)               |
| Not current user                                           | 140 (71.8)           | 119 (61.0)              |
| Alcohol use*                                               |                        |                         |
| Lifetime abstainers                                        | 105 (53.9)           | 121 (62.1)              |
| Former alcohol drinkers                                    | 25 (12.8)            | 25 (12.8)               |
| Current alcohol drinkers                                   | 65 (33.3)            | 49 (25.1)               |

SD: Standard deviation, *p<0.05, **p < 0.001
diagnostic tests, prescription drugs and drug sundries, and other cost such as travel or cost on prescribed specific diet.

**Ethical considerations**

Ethics approval was obtained from the Institutional Ethical Committee (IEC) of the institute in Uttarakhand (IEC/VCSSGMS and RI/003 dated March 21, 2017), where the data collection was done. Permission to use the WHOQOL-BREF questionnaire was also obtained from WHO office. Written informed consent from all the participants was obtained before commencement of the interview.

**Statistical analysis**

Data were entered and analyzed using SPSS version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, New York: IBM Corporation. USA). Chi-square test was applied to measure the association of diabetes with comorbidities, while the strength of association was measured by odds ratio (OR). Multiple linear regression was applied to study the factors associated with direct cost incurred for treatment among diabetics with cardiovascular comorbidities using SPSS and CRAN-R (2.4 version).

**Results**

Table 1 shows the sociodemographic characteristics of the sample population. The mean age of diabetics was 56.8 years with a standard deviation of 12.4 years. Majority of the participants were in ≥60 years of age group, males, and married. It was observed that the proportion of current users of tobacco was higher among nondiabetics in comparison to the diabetics (39% vs. 28.2%).

Table 2 shows the risk of comorbidities of CVS among diabetics and nondiabetics. The overall risk was almost 4 times (OR 3.9; 95% confidence interval [CI] 2.5–6.1) higher among diabetics as compared to the other group, and it was found to be statistically significant. The risk of developing hypertension was 3.9 times (95% CI: 2.4–6.2) and that of MI was 4.4 times (95% CI: 1.5–12.8) in diabetics as compared to nondiabetics. PAD had the highest OR of 17.5 (95% CI 2.2–138.3) among diabetics as compared to nondiabetics.

Table 3 shows that overall QOL scores among diabetics were 92.5 ± 15.6 which was significantly lower as compared to nondiabetics (99.9 ± 11.8).

The overall 6 monthly direct cost among diabetics with CVDs was higher (4890.5 Indian Rupees [INR] vs. 1620.2 INR) than among nondiabetics without CVD ($P < 0.05$). A higher proportion (73.2% vs. 44.6%) of the cost was spent on medication among diabetics with comorbidity as compared to the other group. Though the expenditure on consultation, laboratory tests and other were also higher among diabetics in comparison to other groups, but the difference was not found to be significant [Table 4].

The model could explain 41% of variation in the cost among diabetics with CVDs. The model investigated variables such as gender, religion, income, use of tobacco, use of alcohol, and duration of diabetes. Being Hindu (0.8), married (−1.1), income (12.1), and use of alcohol ($\beta = −13.1$) were significant predictors of direct cost in diabetics with CVDs. It was observed that the use of alcohol had strongest contribution on increase in direct cost [Table 5].

**Discussion**

The present study was conducted with an objective of estimating the proportion and risk of cardiovascular comorbidities among diabetics and nondiabetics. The study also compared the QOL and cost of treatment between diabetics and nondiabetics.

The present study observed that diabetics suffered with various cardiovascular comorbidities and hypertension which ranged from 5.6% to 45.6% for various diseases; the corresponding figures among nondiabetics being significantly lower (0.5%–18.5%). Similar to a study by Lin et al., the most common comorbidity reported was hypertension followed by congestive heart failure, MI, and PAD. Valent et al. in Italy also observed that essential hypertension (39.5%) was the most common comorbidity seen in Type 2 diabetic patients. However, in a study form South India, Mohammed Rashid et al. observed that hypertension was second in the list of comorbidities among diabetic patients, the most common being hyperlipidemia, which could not be assessed for all the patients in the present study.

Gupta observed that CHD and hypertension are the most frequently associated comorbidities with diabetes. The reported prevalence of coexisting diabetes and hypertension varied from 15% to 20% in population. The individual risk of PAD was
Table 3: Comparison of quality of life scores between diabetics and nondiabetics with cardiovascular system comorbidity

| Characteristic | Diabetics with CVS comorbidity (n=98) | Nondiabetics with CVS comorbidity (n=40) |
|----------------|---------------------------------------|-----------------------------------------|
| Physical*      | 23.4±5.2                              | 26.0±3.3                                |
| Psychological* | 23.9±4.4                              | 26.2±3.5                                |
| Social         | 12.1±2.5                              | 12.1±1.6                                |
| Environment*   | 33.0±5.6                              | 35.5±4.8                                |
| Total score*   | 92.5±15.6                             | 99.9±11.8                               |

SD: Standard deviation, CVS: Cardiovascular system, * p < 0.01

Table 4: Comparison of direct costs between diabetics and nondiabetics with cardiovascular system comorbidity

| Characteristic | Diabetics with CVS comorbidity (n=98) | Nondiabetics with CVS comorbidity (n=40) |
|----------------|---------------------------------------|-----------------------------------------|
| Consultation   | 353.1±949.4                           | 284.8±837.9                             |
| Medications*   | 3580.0±7512.6                         | 723.2±1481.4                            |
| Tests          | 415.0±839.711                         | 180.3±547.9                             |
| Any other      | 548.0±1433.2                          | 181.9±799.1                             |
| Total*         | 4890.5±8495.0                         | 1620.2±2751.6                           |

SD: Standard deviation, CVS: Cardiovascular system, * p < 0.001

precise high with an OR of 17.5 in the present study. However, the 95% CI was quite wide indicating the need to study the phenomenon in a larger sample.

The present study reported about four-times higher risk of CVS comorbidities among diabetics as compared to nondiabetics, which is higher than that reported by other studies which reported that all manifestations of CHD, MI, sudden death, and angina pectoris and stroke events are at least twofold more common in patients with Type 2 diabetes than in nondiabetic individuals.\(^{[11-13]}\)

Various instruments such as SF-12, SF-36, RAND 36, EQ5, and health-related QOL (HRQOL) have been used to measure QOL in different studies; we preferred to use the WHOQOL-BREF questionnaire as it is a standardized questionnaire and has been validated internationally as well as nationally.

The QOL scores among diabetics with CVS comorbidities were significantly lower as compared to nondiabetics in our study. Our results were similar to studies conducted by Wee et al., Maddigan et al., and de Visser et al.; however, they used different questionnaires for measuring QOL scores.\(^{[14-16]}\) de Visser et al. in a study from the Netherlands reported a significant negative effect of CVD among diabetic patients on three components (out of eight components) of RAND 36 questionnaire, “impairment due to a physical problem” (β = −10.4, P = 0.01), “mental health” (β = −10.9, P = 0.01), and “health change” (P = −1 0.0, P = 0.01).\(^{[16]}\) Chin et al. in a study from Korea reported the decreased physical scores of QOL when hypertension or CVD were present along with diabetes. They also reported decreased scores in psychological component with the combined comorbidity of hypertension and diabetes, though the study was conducted among elderly.\(^{[17]}\) Wee et al. also found that the presence of a concurrent hypertension, and heart disease reduced SF-36 scores in subjects with diabetes.\(^{[14]}\) Kiadaliri et al. also observed in their study that people with diabetes had lower HRQOL than people without diabetes. Better socioeconomic status and better control of cardiovascular risk factors were reported to be associated with better HRQOL among the patients with diabetes.\(^{[13]}\) Therefore, irrespective of the place of study and instrument used, the QOL scores were found to be adversely affected by the presence of cardiovascular comorbidities among diabetics and therefore controlling the comorbidities would definitely improve the QOL scores.

Studies comparing direct cost of treatment between diabetics and nondiabetics are plenty in number, but those comparing direct cost of treatment among diabetics with cardiovascular comorbidities to nondiabetics with cardiovascular comorbidities are limited.

The present study showed that per month cost of treatment in diabetics with cardiovascular comorbidity (815 INR) was much higher than that, in nondiabetics with cardiovascular comorbidity (270 INR), with maximum expenditure reported on purchase of medicines (INR 597) in comparison to nondiabetics (INR 120). The results of our study matched with that of a study from Chennai, India, where author reported much higher cost of treatment among diabetic patients with cardiovascular comorbidity (13,135 INR) in comparison to nondiabetics (4493 INR). This could be because of the fact that this study was conducted among hospitalized patients and in a private hospital. In comparison to our study, this study showed that major expenditure was on hospital charges (4100 INR) followed by laboratory (3135 INR) and medicine charges (1800 INR).\(^{[19]}\)

Einarson et al. in a systematic review also reported that the cost on treatment increased almost thrice if a diabetic patient had cardiovascular comorbidity. It was also reported that 20%–40% of total cost among diabetics with CVD is because of CVD itself, similarly heart failure contributed to 23% cost in diabetics with heart failure.\(^{[20]}\)

Predictors of cost on multivariate regression analysis, in our study, were religion, marital status, income, and the use of alcohol. Duration of diseases was not found to be significant despite having maximum effect (% = 15) on cost in our study. Other studies have reported duration of diabetes, gender, use of insulin, and number of comorbidities as consistent predictors for direct cost among diabetics with various comorbidities. These differences could be because of different settings, inclusion of indirect cost, cost incurred in IPD, and sample size of the studies.\(^{[21-28]}\)

**Conclusion and Recommendations**

The findings of increased risk of CVS comorbidities among diabetics emphasize the need for screening them for...
these diseases at a regular interval and a “Diabetes CVD collaborative activity component” is proposed to be included in the national program, which provides for regular screening of diabetics and CVD patients for comorbidities and diabetes, respectively.

Limitations of the study

Result of comorbidity of CAD among diabetics in the present study may be underestimated as we collected data based on history and medical records among participants. The results on QOL scores and estimation of direct cost should also be interpreted cautiously as we could not eliminate the effect of diseases from other systems.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Table 5: Multiple linear regression analysis to determine predictors of direct cost among diabetics with cardiovascular diseases

| Predictor variables | β* | SE  | t (P) |
|---------------------|----|-----|------|
| Constant            | 2.4| 0.1 | 17.1 (0.08) |
| Male                | 5.3| 0.2 | 11.1 (0.01) |
| Hindu               | 0.8| 3.0 | 7.5 (0.01) |
| Married             | -1.1| 1.0 | 6.2 (0.03) |
| Education (up to 10*) | -2.0| 1.0 | 2.2 (0.91) |
| Income              | 12.1| 0.1 | 6.3 (0.03) |
| Total family members (≥4) | 7.1| 1.1 | 12.2 (0.19) |
| Use of tobacco      | -1.6| 3.0 | 0.5 (0.67) |
| Use of alcohol      | -13.1| 8.1 | 1.6 (0.01) |
| Duration of DM (years) | 15.0| 1.1 | 5.1 (0.05) |

*Unstandardized coefficients. R²=0.41. SE: Standard error, DM: Diabetes mellitus.