Diabetic complications and poor mental health in the aging population

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INTRODUCTION

Diabetes is a chronic disease characterized by elevated levels of blood glucose. These elevated glucose levels may lead to serious damages to various organs (heart, blood vessels, eyes, kidneys, and nerves) over time. Diabetes is one of the most common causes of blindness, renal failure, neuropathy, myocardial infarctions, stroke, and lower limb amputation in the elderly.

The prevalence of coronary heart disease among diabetes patients with a mean age of 80 years can be up to 44%. Among adults aged ≥60 years, the prevalence of peripheral vascular disease for patients with diabetes is almost twice higher as compared to those without diabetes. The National Health and Nutritional Examination Survey reported a crude prevalence of diabetic retinopathy as 29.5% among diabetic patients aged ≥65 years. The prevalence of chronic kidney disease is consistently higher among patients with diabetes. Among adults aged ≥75 years, about 1/3 of new cases of end-stage renal disease are caused by diabetic nephropathy.

Depression is linked to the hypothalamic-pituitary-adrenal axis dysregulation, sympathetic nervous system activation, and proinflammatory and procoagulation markers among older people.

ABSTRACT

Introduction: Diabetes is a known risk factor for mental health disorders in the older population. This effect can be due to direct impact of chronic disease or indirectly due to the impact of diabetic complications. This study aims to assess the association of individual diabetic complications with depression, generalized anxiety disorder (GAD), cognitive impairment, and quality of life (QOL) in older diabetic population. Materials and Methods: A cross-sectional study was performed in Geriatric Medicine OutPatient Department from November 2014 to June 2016. One hundred and eighty diabetic patients were diagnosed using the American Diabetes Association (ADA)-2015 diagnostic criteria and were included in the study. They were assessed for the presence of diabetic complications (diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, coronary artery disease, and cerebrovascular disease (CVD) as per the ADA-2015 guidelines. They were also subjected to assessment for the presence of depression, GAD, cognitive impairment, and health-related QOL by using Geriatric Depression Scale, Mini-International Neuropsychiatric Interview, Montreal Cognitive Assessment, and WHOQOL-BREF scale, respectively. The Chi-square test/Fisher's exact test and unpaired t-test were used for the statistical analysis. Results: Diabetic neuropathy and CVD in diabetes have higher risk of depression (49.3% vs. 27%; P = 0.002) and cognitive impairment (82.4% vs. 50.9%; P = 0.013), respectively, as compared to those with diabetes without such complications. Patients with diabetic nephropathy have poor environmental domain QOL (68.02 ± 15.16 vs. 72.82 ± 14.86; P = 0.040) as compared to those without diabetic nephropathy. Conclusions: Diabetic complications in old age are independently associated with increased risk of mental health disorders and impaired health-related QOL. Thus, patients with diabetic complications should be specifically assessed and managed for mental health disorders in addition to the management of metabolic abnormalities.

Key words: Diabetic complications, elderly, health-related quality of life, mental health disorders, older people
patients with coexisting cardiovascular disorders.[4] Perhaps, these pathophysiologic responses also have similar roles in the progression of microvascular and macrovascular complications in diabetic patients. Major depression in diabetes is associated with increased risk of diabetic complications (both microvascular and macrovascular) over longitudinal follow-up, even after adjusting for the severity of diabetes and self-care activities.[5]

A diagnosis of diabetes may induce anxiety because individuals may perceive that their disease requires undesirable lifestyle changes, causes them to lose control over their health and will lead to various complications, such as diabetic retinopathy, neuropathy, sexual dysfunction, and macrovascular complications.[6] Peyrot et al. demonstrated that individuals with anxious coping styles (i.e., avoidance, escape, and denial) showed reduced adherence to diabetes self-care regimens and poorer glycemic control, which, in turn, may lead to increased diabetic complications.[7]

Microvascular damage may lead to cerebral microinfarcts and cerebral white matter lesions. Previous studies have shown that the vascular complications of diabetes (such as retinopathy) are the most important predictors for the cognitive decline.[8]

Among diabetic individuals, a key factor influencing the quality of life (QOL) includes the degree and nature of diabetes-related complications experienced by patients. Thus, the prevention of these complications is critical to reduce the decline in QOL for people with diabetes.[9]

Most of the previous studies have either focused only on depression or anxiety disorder or cognition, but studies assessing all of them comprehensively along with QOL together in diabetes are limited. Main aims of this study were to find the association of diabetes complications with depression, generalized anxiety disorder (GAD), cognitive impairment, and QOL in older diabetics in the Indian population. This study is a subgroup analysis of previously published study in “Journal of geriatric mental health” that compared the frequency of Depression, GAD, cognitive impairment, and QOL in older diabetics as compared to nondiabetic in the Indian population.[10]

**MATERIALS AND METHODS**

In this cross-sectional descriptive study, 180 cases of diabetes diagnosed as per the American Diabetes Association (ADA)-2015 criteria were recruited from the Geriatric Medicine Out Patient Department of a tertiary care hospital between November 2014 and June 2016. Patients were recruited using nonprobability sampling method, where first two cases fulfilling the inclusion and exclusion criteria were recruited daily. Inclusion criteria were diabetes diagnosed as per the ADA-2015 criteria and willingness to participate in the study. Exclusion criteria were inability to communicate for the complete assessment and withdrawal of consent. Permission for ethical clearance was obtained from the local ethical body of the institution. After recruitment, patients were subjected to detailed assessment, which included demographic details, standard clinical assessment, and other health issues etc.

For diagnosing diabetic complications, various tools were used, as summarized in Table 1. Other comorbidities such as hypertension and chronic obstructive pulmonary disease (COPD) were also enquired. Mental health assessment was performed using validated scales, as summarized in Table 1.

To compare the association of diabetic complications with mental health disorders (depression, GAD, and cognitive dysfunction) and QOL, the Chi-square test/Fisher’s exact test and unpaired t-test were used, respectively. Correlation analysis was used to compare the two continuous variables. Multivariate logistic and multivariate regression analysis was used to find whether various factors are the independent risk factors for the outcomes in diabetes.

**Table 1: Diagnosis of diabetic complications and mental health disorders**

| Variable               | Tool used                              | Comments                                                                 |
|------------------------|----------------------------------------|--------------------------------------------------------------------------|
| Diabetic retinopathy   | Indirect ophthalmoscopy (by ophthalmologist after dilating the pupils) | Positive = Any evidence of diabetic retinopathy (NPDR or PDR)             |
| Diabetic nephropathy   | UACR (early morning urine spot sample) | Microalbuminuria = UACR (microgram/milligram) → 30-299                   |
| Diabetic neuropathy    | Clinical neurological assessment       | Macroleukinuria = UACR (microgram/milligram) → > 299                     |
| CAD                    | History of acute chest pain ECG (presence of ‘q’ waves) 2D ECHO (presence of regional wall motion abnormalities) | Positive = Both microleukinuria and macroleukinuria                       |
| CVD                    | History of TIA/stroke CT and MRI      | 2D ECHO = Used only if already done for indications other than research purpose |
| Depression             | 15 items GDS[11]                       | CT and MRI = Was used only if already done for indications other than research purpose |
| GAD                    | MINI[12]                               | Score > 5 = Suggestive of depression                                     |
| Cognitive impairment   | MoCA[13]                               | Validated instrument for screening depression in elderly                  |
| QOL                    | WHOQOL-BREF[14]                        | Score < 26 = Cognitive impairment                                         |

NPDR: Nonproliferative DR, PDR: Proliferative DR, UACR: Urine albumin/creatinine ratio, CAD: Coronary arterial disease, CVD: Cerebrovascular disease, GAD: Generalised anxiety disorder, WHOQOL-BREF: World Health Organisation Quality of Life-BREF, MRI: Magnetic resonance imaging, GDS: Geriatric Depression Scale, MoCA: Montreal Cognitive Assessment, MINI: Mini International Neuropsychiatric Interview, CT: Computed tomography, TIA: Transient ischemic attack, ECG: Electrocardiogram, 2D: Two-dimensional, ECHO: Echocardiography
RESULTS

The mean age of diabetic patients in this study was 64.68 ± 4.89. Among them, around 60% were male. Cases were distributed evenly in all the strata of socioeconomic status. Mean body mass index (BMI) was 24.11 ± 4.07 [Table 2]. The most common comorbidity observed was hypertension (64.4%) followed by benign prostate hyperplasia and COPD. Only 16.7% of diabetic patients had no other comorbidity. A total of 69.4% diabetic patients had some form of diabetic complications. The frequency of diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, coronary artery disease (CAD), and cerebrovascular disease (CVD) was 32.8%, 36.1%, 38.3%, 19.4%, and 9.4%, respectively [Table 3].

On comparing diabetics patients for the association of diabetic complications with sociodemographic characters, none of these characters were significantly associated with diabetic complications [Supplementary Table 1].

On comparing diabetic patients for the association of mental health disorders (depression, GAD, and cognitive dysfunction) and QOL with demographic characters (age, gender, socioeconomic status, occupation, education, family income, marital status, and BMI), none of these characters were significantly associated with any mental health disorder or poor QOL [Supplementary Tables 2 and 3].

Diabetic neuropathy was associated with increased risk of depression as compared to those without diabetic neuropathy in diabetic patients (49.3% vs. 27%; P = 0.002) [Table 4]. There was no significant association of any diabetic complication with GAD [Table 4]. CVD was associated with increased risk of cognitive dysfunction as compared to those without CVD in diabetes patients (82.4% vs. 50.9%; P = 0.013) [Table 4].

Environmental domain QOL was poor in a patient with diabetic nephropathy as compared to those without diabetic nephropathy (68.02 ± 15.16 vs. 72.82 ± 14.86; P = 0.040) [Table 5].

On further analysis, mean scores of the Geriatric Depression Scale (GDS) had weakly negative correlation with a mean score of Montreal Cognitive Assessment (correlation coefficient = −0.180, P = 0.016). Furthermore, diabetic neuropathy was significantly associated with higher value of GDS scores as compared to those without diabetic neuropathy (P = 0.008) [Supplementary Table 4].

DISCUSSION

Diabetes is an epidemic of the 21st century. It not only impairs physical health of the individual but also hampers mental health, social health, and financial health of the individual. Older patients are even more vulnerable as diabetic complications are common in old age.

In this study, the mean age in diabetic is 64.68 ± 4.89 years. Most of them (72.8%) are ≤65 years old. This trend is similar to what is seen in urban slums of Delhi where the incidence of diabetes increases initially with age but declines thereafter[13]. Even though the peak age, when the incidence starts declining is earlier than western countries. This can also be biased due to the social factors in India, where relatively younger elderly reach more to tertiary hospitals for treatment, whereas very elderly usually...
Table 4: Association of diabetic complications with depression, generalized anxiety disorder, and cognitive dysfunction in diabetes

| Variables | Depression | GAD | Cognitive dysfunction |
|-----------|------------|-----|-----------------------|
|           | Frequency (percentage in row) | Frequency (percentage in row) | Frequency (percentage in row) |
| Present (n = 125) | 48 (38.4) 77 (61.6) 0.229 | 14 (11.2) 111 (88.8) 0.339 | 72 (57.6) 53 (42.4) 0.132 |
| Absent (n = 55) | 16 (29.1) 39 (70.9) (1.445) | 9 (16.4) 46 (83.6) (0.914) | 25 (45.5) 30 (54.5) (2.267) |
| Diabetic retinopathy | | | |
| Present (n = 59) | 25 (42.4) 34 (57.6) 0.182 | 4 (6.8) 55 (93.2) 0.092 | 35 (59.3) 24 (40.7) 0.307 |
| Absent (n = 121) | 39 (32.2) 82 (67.8) (1.780) | 19 (15.7) 102 (84.3) (2.833) | 62 (51.2) 59 (48.8) (1.043) |
| Diabetic nephropathy | | | |
| Present (n = 65) | 26 (40.0) 39 (60.0) 0.349 | 5 (7.7) 60 (92.3) 0.124 | 38 (58.5) 27 (41.5) 0.355 |
| Absent (n = 115) | 38 (33.0) 77 (67.0) (0.877) | 18 (15.7) 97 (84.3) (2.361) | 59 (51.3) 56 (48.7) (0.856) |
| Diabetic neuropathy | | | |
| Present (n = 69) | 34 (49.3) 35 (50.7) 0.002 | 11 (15.9) 58 (84.1) 0.316 | 42 (60.9) 27 (39.1) 0.139 |
| Absent (n = 111) | 30 (27.0) 81 (73.0) (9.192) | 12 (10.8) 99 (89.2) (1.005) | 55 (49.5) 56 (50.5) (2.194) |
| CAD | | | |
| Present (n = 35) | 14 (40.0) 21 (60.0) 0.541 | 4 (11.4) 31 (88.6) 0.790 | 19 (54.3) 16 (45.7) 0.958 |
| Absent (n = 145) | 50 (34.5) 95 (65.5) (0.375) | 19 (13.1) 126 (86.9) (0.071) | 78 (53.8) 67 (46.2) (0.003) |
| CVD | | | |
| Present (n = 17) | 6 (35.3) 11 (64.7) 0.981 | 2 (11.8) 15 (88.2) 0.895 | 14 (82.4) 3 (17.6) 0.013 |
| Absent (n = 163) | 58 (35.6) 105 (64.4) (0.001) | 21 (12.9) 142 (87.1) (0.017) | 83 (50.9) 80 (49.1) (6.121) |

Table 5: Association of diabetic complications with quality of life in diabetes

| Variable | Present | Absent | t-test value | P |
|----------|---------|--------|--------------|---|
| DM complication | | | | |
| Physical domain QOL | 59.57±16.72 | 57.84±18.13 | 0.624 | 0.534 |
| Psychological domain QOL | 64.47±20.20 | 69.33±18.66 | −1.520 | 0.130 |
| Social domain QOL | 74.18±17.74 | 73.93±18.66 | 0.088 | 0.930 |
| Environmental domain QOL | 70.05±15.31 | 73.44±14.47 | −1.390 | 0.166 |
| Diabetic retinopathy | | | | |
| Physical domain QOL | 58.85±16.79 | 59.13±17.36 | −0.104 | 0.917 |
| Psychological domain QOL | 64.71±19.30 | 66.56±20.11 | −0.587 | 0.558 |
| Social domain QOL | 73.53±18.75 | 74.39±17.66 | −0.302 | 0.763 |
| Environmental domain QOL | 67.98±16.09 | 72.60±14.42 | −1.938 | 0.054 |
| Diabetic nephropathy | | | | |
| Physical domain QOL | 59.26±15.41 | 58.91±18.10 | 0.131 | 0.896 |
| Psychological domain QOL | 63.94±18.63 | 67.10±20.44 | −0.027 | 0.306 |
| Social domain QOL | 75.71±18.27 | 73.20±17.82 | 0.899 | 0.370 |
| Environmental domain QOL | 68.02±15.16 | 72.82±14.86 | −2.068 | 0.040 |
| Diabetic neuropathy | | | | |
| Physical domain QOL | 59.96±16.49 | 58.47±17.57 | 0.656 | 0.572 |
| Psychological domain QOL | 65.16±22.19 | 66.45±18.27 | −0.424 | 0.672 |
| Social domain QOL | 73.90±17.74 | 74.23±18.20 | −0.121 | 0.903 |
| Environmental domain QOL | 71.58±15.31 | 70.77±15.03 | 0.347 | 0.729 |
| CAD | | | | |
| Physical domain QOL | 61.51±17.39 | 58.44±17.07 | 0.060 | 0.342 |
| Psychological domain QOL | 63.69±18.37 | 66.50±20.17 | 0.876 | 0.452 |
| Social domain QOL | 71.46±19.83 | 74.74±17.51 | 2.725 | 0.333 |
| Environmental domain QOL | 69.66±15.98 | 71.43±14.92 | 0.025 | 0.335 |
| CVD | | | | |
| Physical domain QOL | 54.24±17.11 | 59.54±17.11 | 0.017 | 0.225 |
| Psychological domain QOL | 67.12±27.01 | 65.83±19.01 | 7.119 | 0.800 |
| Social domain QOL | 78.59±20.42 | 73.64±17.71 | 0.805 | 0.281 |
| Environmental domain QOL | 72.71±16.51 | 70.91±14.99 | 0.379 | 0.643 |

CAD: Coronary artery disease; CVD: Cerebrovascular disease; GAD: Generalised anxiety disorder

continue their treatment from primary or secondary care hospitals and rarely report to tertiary care hospitals. In this study, majority are male, which is different from what is seen by the International Diabetes Federation[16] where diabetes is equally distributed in both the genders. This can be biased due to the patriarchal society where females...
often have restricted access to health care system. Around 56% are overweight or obese in this study, suggesting that Indian elderly diabetics are thinner than their Western counterparts, where the incidence of obese or overweight in elderly diabetic is 84.7%.[17]

In this study, two-thirds of diabetic patients have some form of diabetic complications (either microvascular or macrovascular). The frequency of diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy is 32.8%, 36.1%, and 38.3%, respectively. Rema et al.,[18] Unnikrishnan et al.,[19] and Pradeepa et al.[20] observed the prevalence of diabetic retinopathy, microalbuminuria, and diabetic neuropathy to be 20.8%, 26.9%, and 26.1% respectively, in the Chennai population. The frequency of CAD and CVD in this study is 19.4% and 9.4%, respectively, in diabetes, which is similar to their western counterparts.[21]

Vision loss increases falls risk in older individuals, which may lead to functional disability and potentially result in older patients feeling isolated and being more vulnerable to depression.

Diabetic neuropathy leads to approximately two times increased risk of depression than those without diabetic neuropathy in diabetes patients (49.3% vs. 27%). This relationship between diabetic neuropathy and depressive symptoms can be due to patients’ subjective experiences of neuropathic pain, reduced feeling in the feet and unsteadiness, and the presence of a neuropathic foot ulcer. Thus, neuropathy itself may be an independent risk factor for depression in diabetic patients. Previous studies have also predicted diabetic neuropathy as one of the strongest factors related to depression in diabetes.[22] In older diabetic patients, peripheral neuropathies have detrimental effects on stability, sensorimotor function, gait, and activities of daily living.[23]

GADs are not specifically associated with any diabetic complication. Although previous studies have discovered the association between anxiety and diabetic complications, most of those studies have used the screening tools for assessing the anxiety symptoms rather than specifically diagnosing GAD.[24]

CVD leads to ~60% increased risk of cognitive dysfunction as compared to those without CVD in diabetes patients (82.4% vs. 50.9%). Multiple pathophysiologica mechanisms contribute to cognitive dysfunction. Although the main changes in the brain include cerebral infarcts, cognitive dysfunction can be due to factors beyond acute infarcts. Cerebral white matter lesions and silent brain infarcts are considered to be risk factors for dementia.[25] Previous studies have shown diabetes as a risk factor dementia (vascular and neurodegenerative) with approximately two-fold increased risk.[26] Not having diabetes in lifetime can be associated with preserved cognitive function in women >80 years of age.[27]

The mean scores of environmental domain QOL in a patient with diabetic nephropathy are poor when compared with those without diabetic nephropathy. In previous studies, complications of diabetes are the most important disease-specific determinant of QOL.[28] Diabetic nephropathy itself may worsen environmental QOL through various mechanisms. In WHOQOL-BREF, environmental domains questionnaire includes “How safe do you feel in your daily life?” and “Have you enough money to meet your needs?” In diabetic nephropathy, patients feel that their kidneys are failing, and they will need lifelong dialysis, and hence, they have a sense of insecurity about their future. Furthermore, they have to spend a lot more money for dialysis and medications for chronic kidney disease, which may have a financial impact on patient. Thus, diabetic nephropathy may directly impair the QOL in diabetic patients.

The strength of this study is adequate sample size and comprehensive evaluation of mental health disorders allowing the assessment of various mental health issues comprehensively, unlike various previous studies that assessed mental health issues in isolation.

Limitations of the study are the inability to establish the causative relation between diabetic complications and mental health for which a longitudinal study is needed. Results cannot be generalized to other populations or to community settings as this study includes patients from a single center of tertiary care hospital.

CONCLUSIONS

In summary, this study has shown that diabetic complications such as diabetic neuropathy, CVD, and diabetic nephropathy are risk factors for depression, cognitive dysfunction, and the environmental domain of impaired QOL. Although all the diabetic patients should have a comprehensive mental health check-up routinely, in Indian scenario, physician may not spend enough time for diagnosing mental health disorders in all diabetic patients due to time constraints. Thus, at least, patients with diabetic complications should be screened for mental health disorders as they are more likely to have these mental disorders than diabetic without any complications.

This study has shown that diabetic complications are at increased risk of mental health disorders when compared with those without complications, but there are no studies suggesting whether screening and early treatment of these mental disorders have beneficial effects on the level of glycemic control, adherence to treatment, morbidity, and overall mortality. Future studies are required to study these outcomes.

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There are no conflicts of interest.
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