Review Article

Retinal microvascular abnormalities and cognitive dysfunction in older patients with Type-II diabetes mellitus

Goyal Dimple*, Johal Sunmeet, Kosey Sourabh

Department of Pharmacy Practice, ISF College of Pharmacy, Moga, Punjab, India

Correspondence:
Goyal Dimple, Department of Pharmacy Practice, ISF College of Pharmacy, Moga, Punjab, India.
E-mail: dimplegyl1@gmail.com

How to cite this article: Dimple G, Sunmeet J, Sourabh K. retinal microvascular abnormalities and cognitive dysfunction in older patients with Type-II diabetes mellitus. Pharmaspire 2021;13(4):140-143.

Source of Support: Nil,

Conflicts of Interest: None declared

ABSTRACT

The main aim of this prospective study was to determine whether several parameters of retinal microvascular abnormality were related to cognitive ability and to estimate cognitive impairment in people with Type 2 diabetes mellitus and was carried out for six months in Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab. Among 75 study participants, 66.7% were males and 33.3% were females. The mean age of the patients was 63.95 years. A large number of the study population, up to 38.6% suffered diabetes from 11 to 15 years where 40% had early macular edema due to retinopathy. The majority of study participants, up to 33.33% were found not to have a cognitive impairment, 40% had mild cognitive impairment, 20% had moderate cognitive impairment, and 6.64% were to have severe cognitive impairment. The Pearson Correlation between age, duration of diabetes, Stage of Binocular digital retinal photography and Cognitive Impairment was found to be Strong ($r = 0.690, 0.720, 0.675, 0.651$) and statistically significant ($P < 0.01$) at 95% Confidence Interval. These results conclude that the prevalence of retinal microvascular abnormalities was higher in males than females and shows a strong correlation between age, duration of diabetes, Stage of Binocular digital retinal photography, and Cognitive Impairment. This study suggests that people with a history of diabetes and retinal microvascular abnormalities are prone to reduced cognitive ability and cognitive decline. However, further investigation is required to confirm the relation between retinal microvascular disease and cognitive decline.

Keywords: Cognitive dysfunction, diabetic retinopathy, retinal microvascular abnormalities, Type-2 diabetes mellitus

INTRODUCTION

A metabolic disorder diabetes mellitus characterized by hyperglycemia occurs due to imperfect insulin secretion and ineffective insulin action stated as Type 1 and Type 2 diabetes mellitus, respectively. According to IDF Atlas, edition 8th of 2017, about 352 million populations suffer from diabetes; of which around 57% is about 47 million people remain undiagnosed. Diabetic retinopathy is one of the major microvascular complications of diabetes mellitus. Mazhar *et al*. (2011) explain the association of mild tomoderate vision loss, non-proliferative diabetic retinopathy and diabetic macular edema with a reduction in the quality of life.[1] According to the International Association on the Prevention of Blindness (IAPB), 145 million people had some form of DR and 45 million people suffered from vision-threatening DR in 2015.[2,3] 35% is the prevalence of any retinopathy in persons with diabetes while proliferative (vision-threatening) retinopathy is 7%.[4] Other factors that increase the risk of retinopathy are chronic hyperglycemia, nephropathy, hypertension, and dyslipidemia.[5-9] A study conducted in Sweden states that 10 million EUROs are consumed by diabetic retinopathy in health care expenditures.[10] According to 2014 data, the cost of diabetic retinopathy is 233 EUROs, while the mean cost of DME went from705 EUROs to 4,200 EUROs from 2007 to 2014 in Spain respectively.[11] According to Lightamn and Towler, (2003), in patients with type 1DM, the proliferative diabetic retinopathy

Access this article online	
Website: www.isfcppharmaspire.com	**P-ISSN:** 2321-4732 **E-ISSN:** XXXX-XXXX

accounts for the most common form of vision-threatening diabetic retinopathy whereas diabetic macular edema is the most common cause of vision loss in patients with type 2 diabetes mellitus.[12]

Aims of the study

- To determine whether several parameters of retinal microvascular abnormality were related to cognitive ability or not in people with Type 2 diabetes.
- To estimate cognitive impairment (based solely upon cognitive test performance) in people with Type 2 diabetes.

Objectives of the study

- To determine the association of the presence of diabetic retinopathy and severity of diabetic retinopathy with cognitive ability and cognitive impairment.
- To determine the independence of associations between the retinal microvascular abnormalities and cognitive function after diabetes control.

METHODS

A prospective observational study was conducted after approval from IEC. The study was conducted in Medicine wards I, II, III at Guru Gobind Singh Medical College Hospital and Research Center, Faridkot, Punjab six months. Data were collected from patient case sheets, laboratory test reports, and patient interviews in the specially designed data collection form after taking the written consent from the patient diagnosed with diabetic retinopathy. Patients enrolled in this study were recruited based on inclusion and exclusion criteria after obtaining written consent from patients diagnosed with Retinopathy. The case record form did not contain the name of the patient, to protect the patient's identity at all points in time.

Inclusion criteria

- Patients diagnosed with diabetes Mellitus with complications (retinopathy) are both admitted inpatient and outpatient follow up.
- Both the genders with age between 51 and 75years.

Exclusion criteria

- Patient age less than 50year.
- The patient not willing to participate in the study.
- Pregnant and lactating mothers.

Among 75 study participants, 66.7% were male and 33.3% were female. The mean age of the patients was found to be 63.95 years. A large number of the study population up to 38.6% suffered diabetes from 11 to 15 years and 40% had early macular edema due to retinopathy. There was a strong correlation between age, duration of diabetes, Stage of Binocular digital retinal photography, and Cognitive Impairment. This suggests that people with a history of diabetes and retinal microvascular abnormalities are prone to reduced cognitive ability and cognitive decline.

RESULTS

This study was conducted at Guru Gobind Singh Medical College and Hospital, Faridkot in the medicine department for 6 months from Aug. 2019 to Feb. 2020. The sample size of the study was 131. Out of 131 patients, 75 were enrolled for analysis. 56 patients were excluded from the analysis because of missing values. SPSS version 16 was used to perform the analysis. The confidence interval of the study was selected 95% with a cut-off interval ($P = 0.05$) as a significant level. The sample size of the study was calculated through software, Epi info made by the Centre for Disease Control and Prevention (CDC) in Atlanta (US). The data were coded, checked for competencies, and entered in SPSS for further analysis. A descriptive study was conducted to describe basic features of data in the study and to provide simple summaries about the sample and the measures. The descriptive analysis includes mean, standard deviation (for normally distributed data), and median (for not normally distributed data).

a. Age distribution of patients: Out of 75 patients, 11 (14.67%) patients were significantly higher in the age group, 71-75 years. 10 (13.33%) patients were less significant in the age group 51–55. The mean age (mean ± S.D) of the patients was 63.43 ± 6.35years, and the median age was 65.5 years.
b. Gender distribution of patients: Out of the 75 studied patients, 67.1% (50) patients were male, and 32.9% (25) were female. Test of proportion showed that the male patients were slightly more than the female patients.
c. Duration of diabetes: Mean and Standard deviation for the duration of diabetes (mean ± S.D) of the patients was 26.13 ± 9.57, and the median was 15.81. Test of proportion showed 25 (33.33%) patients were between 6 and 10 years, 30 (40%) patients were between 11 and 15 years, 15 (20%) patients were between 16 and 20 years, and 5 (6.64%) patients were between 21 and 25 years.
d. Distribution of glycated hemoglobin inpatients: On the evaluation, all 75 patients having the high glycated hemoglobin level in their body. Total numbers of the patient are 75, and all the patient having diabetes and increase glycated hemoglobin level so that the percentage is 100%.
e. Stage of Binocular digital retinal photography: Out of the 75 studied patients, 25 (33.3%) of patients are having early macular edema, 19 (25.4%) of the patient are having advance macular edema, 15 (20%) of the patient are developing the new vessels and bleeding due to retinopathy, 15 (20%) having are having the retinal stage that is bleeding and edema, and 1 (1.3%) of patients are suffering from the severe bleeding stage of retinopathy. The mean and the standard deviation (mean ± SD) of the patients were 15 ± 2.04, and the median was15.
f. Distribution of the hospital anxiety and depression scale: Out of the 75 studied patients, 30 (40%) patients do not have hospital anxiety and depression, 25 (33.33%) patients are having a possible case of hospital anxiety and depression, and 20 (26.67%) patient are the probable cases of hospital anxiety and depression. The mean and the standard deviation of the patient were 25 ± 1.414, and the median was 25.
g. Distribution of the mini-mental state examination: Out of the 75 studied patients, 30 (40.0%) do not have a cognitive impairment,

25 (33.33%) are having a mild cognitive impairment, and 20 (26.67%) are having severe cognitive impairment. The mean and the standard deviation of the patient were 25 ± 0.812, and the median was 25.

h. Distribution of the mill hill vocabulary scale: Out of the 75 studied patients, 27 (38.6%) patients do not have a cognitive impairment, 14 (20%) are having a mild cognitive impairment, 19 (27.1%) are having a moderate cognitive impairment, and 10 (14.3%) are having severe cognitive impairment. The mean and the standard deviation of the patient were 18.75±0.812, and the median was 22.5.

i. Distribution of the Wechsler memory scale-III: logical memory test (Immediate and Delayed recall): Out of the 75 studied patients, 25 (33.33%) patients do not have a cognitive impairment, 30 (40%) are having mild cognitive impairment, 15 (20%) are having the moderate cognitive impairment, and 5 (6.64) are having the severe cognitive impairment. The mean and the standard deviation of the patient were 18.75 ± 0.812, and the median was 22.5.

j. Distribution of the trial-making test part –B: Out of the 75 studied patients, 30 (40%) patients do not have a cognitive impairment, 25 (33.33%) are having mild cognitive impairment, and 20 (26.67%) are having severe cognitive impairment. The mean and the standard deviation of the patient were 25±0.810, and the median was 25.

k. Distribution of the Wechsler memory scale - III: Faces and family pictures test (Immediate and Delayed recall): Out of the 75 studied patients, 25 (33.33%) patients do not have a cognitive impairment, 30 (40%) are having a mild cognitive impairment, 15 (20%) are having a moderate cognitive impairment, and 5 (6.64%) are having severe cognitive impairment. The mean and the standard deviation of the patient were 18.75 ± 0.812, and the median was 22.5.

l. Distribution of the Wechsler adult intelligence scale - III: Matrix reasoning test: Out of the 75 studied patients, 25 (33.33%) patients do not have a cognitive impairment, 30 (40%) are having mild cognitive impairment, 15 (20%) are having moderate cognitive impairment, and 5 (6.64%) are having severe cognitive impairment. The mean and the standard deviation of the patient were 18.75 ± 0.812, and the median was 22.5.

m. Distribution of the Wechsler adult intelligence scale - III: Digit symbol - coding test: Out of the 75 studied patients, 30 (40%) patients do not have a cognitive impairment, 25 (33.33%) patients having a mild cognitive impairment, and 20 (26.67%) are having severe cognitive impairment. The mean and the standard deviation of the patient were 25 ± 0.810, and the median was 25.

n. Distribution of the Borkowski verbal fluency test: Out of the 75 studied patients, 25 (33.33%) patients do not have a cognitive impairment, 30 (40%) are having mild cognitive impairment, 15 (20%) are having moderate cognitive impairment, and 5 (6.64%) are having severe cognitive impairment. The mean and the standard deviation of the patient were 18.75±0.812, and the median was 22.5.

o. Distribution of the Wechsler adult intelligence scale - III: Letter - number sequencing test: Out of the 75 studied patients, 25 (33.33%) do not have a cognitive impairment, 30 (40%) are having mild cognitive impairment, 15 (20%) are having moderate cognitive impairment, and 5 (6.64%) are having the severe cognitive impairment. The mean and the standard deviation of the patient were 18.75 ± 0.812, and the median was 22.5.

DISCUSSION

We acknowledge that this type of study has certain limitations such as small sample size and there may be the presence of confounding factors because of this the results cannot be generalized to the overall population. For analysis of cognition dysfunction, this study has only focused on verbal fluency, not on the other domains of cognitive function affected by the disease. However, it should closely approximate the relationship between retinal microvascular abnormalities and cognitive dysfunction in the case of a scenario in the Punjab region. In this representative population of older people with type 2 diabetes mellitus, the majority of the study participants up to 66.7% was found to be males as compared to their female counterparts up to 33.3% which is also similar to findings were reported in a study conducted in the United Kingdom which suggested that a significant dose-response relationship was found only in men and for individual tests of verbal fluency, information processing speed and mental flexibility (but not memory and nonverbal reasoning). These associations persisted after adjustment for estimated pre-morbid cognitive ability (vocabulary scores), suggesting that in men, DR was not only associated with cognitive ability in later life but also with increased estimated lifetime cognitive decline. Test of proportion showed most of the patients 26.6% were significantly higher in the age group 71–75 years which was also reported in various other studies. The Pearson Correlation between age and Cognitive Impairment was found to be Strong, $r = 0.690$, and statistically significant ($P < 0.01$) at a 95% Confidence Interval. The prevalence of diabetic retinopathy was higher in urban patients than the rural patient which was also reported in a study conducted in South India, Lifestyle and ethnicity can be a major factors in this difference. Surprisingly this factor has not been well studied by various studies conducted in India and other parts of the world. A large proportion of the study population up to 40% suffered diabetes mellitus from 11 to 15 years. The Pearson Correlation between the duration of diabetes and Cognitive Impairment was found to be Strong, $r = 0.720$, and statistically significant ($P < 0.01$) at a 95% Confidence Interval. The duration of diabetes that is closely related to age, which may affect cognition and has been investigated in several recent epidemiological studies is the period an individual has had diabetes. Such duration of diabetes is normally calculated by subtracting the age at diagnosis from the current age. Because people with diabetes may have the disease many years before diagnosis, the true duration of diabetes is often difficult to estimate precisely and may therefore be underestimated. Despite these difficulties, there is increasing evidence from recent studies suggesting longer duration of diabetes may be an important risk factor for cognitive dysfunction in older people with Type 2 diabetes mellitus. The Pearson Correlation between glycated hemoglobin and Cognitive Impairment was found to be Strong, $r = 0.675$, and statistically significant ($P < 0.01$) at a 95% Confidence Interval. The Pearson Correlation between Stage of Binocular digital retinal photography and Cognitive Impairment was found to be Strong, $r = 0.651$, and statistically significant ($P < 0.01$)

at 95% Confidence Interval which is similar to the findings of other studies.

CONCLUSION

This study has found that the prevalence of retinal microvascular abnormalities was higher in males than in female counterparts. There was a strong correlation between age, duration of diabetes, Stage of Binocular digital retinal photography, and Cognitive Impairment. These suggest that people with a history of diabetes and retinal microvascular abnormalities are prone to reduced cognitive ability and cognitive decline. However, further investigation is required to confirm the relation between retinal microvascular disease and cognitive decline.

Direction for future research

- Assessment of the relationship between the residence/locality of patients with T2DM and retinal microvascular abnormalities should be explored.
- Studies on preventive strategies should also be considered as a direction for future research

Limitations of the study

Keeping in mind, the limitations of the current study are fewer times period, lesser number of subjects, and the shorter duration of follow-up.

ACKNOWLEDGMENT

This article becomes a reality with the kind support and help of many individuals. We would like to extend our sincere thanks to all of them. It is a dream for any aspiring person to study, gain knowledge, and use this hard-earned treasure to change destiny. With high honor and intense interest, it's our privilege to acknowledge genuine gratitude to our supervisor Mr. Sourabh Kosey, Associate Professor, for his motivation and enormous assistance he provided to us that developed the enthusiasm to accomplish our work very well.

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