ORIGINAL ARTICLE

Association of Dementia in Metformin Users With Type 2 Diabetes (T2DM) at Tertiary Care Hospital in Karachi

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ABSTRACT

Objective: To determine the association of dementia in metformin users with Type 2 Diabetes presenting at Tertiary Care Hospital in Karachi

Methodology: This cross-sectional study was carried out using non-probability purposive sampling technique in the outpatient department of Diabetes clinic at JPMC, within a period of 6 months after approval from Institutional Review Board (IRB) of JPMC. A total of 83 out of 350 patients of both genders with type 2 diabetes mellitus (T2DM), using metformin, between the ages of 18 and 75, and selected by Mini Mental State Examination (MMSE), were included in the study and were evaluated for association.

Results: Total 350 patients were evaluated by MMSE in which 83 patients were found to have dementia. More women (50) 62.2 % had dementia compared to males (33) 39.8% with a significant p-value of 0.015. Our study showed the risk of mild to moderate dementia rising with the increase in the mean age 47.29±7.63 years to 52.50±8.85 years respectively with significant p-value of 0.006. The risk of dementia increased with the duration of diabetes as patients with mean 3.74±2.32 years of diabetes had mild dementia whereas patients with mean 9.20±3.91 years of diabetes had moderate dementia with a significant p-value of 0.001.

Conclusion: Finding of this study concludes that more females suffer from dementia in metformin users with T2DM and the risk of dementia increases with age and with the duration of diabetes.

Key Words: Age, dementia, gender, metformin, type 2 diabetes mellitus (T2DM)

INTRODUCTION

Dementia is a disorder in which there is a decay in memory, thinking, conduct and the capacity to do regular performance and activities[1]. Roughly 47 million people are living with dementia globally and this number could triple by 2050[2,3]. Dementia has become a global health concern[4]. Despite the fact that it is a major health issue, the response (treatment and slowing its progression) is slower in developing countries like Pakistan. Previous studies in our country show lack of knowledge about the disease which makes people consider dementia to be age related changes[5]. The over

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all expenses of dementia were assessed to be US$818 billion in 2015, about 35% increase from 2010, in which 86% of total expenses happened in developed nations. The limit of US$1 trillion was expected to be crossed by 2018[6]. Expenses of casual consideration and immediate expenses of social consideration still contribute comparable extents of absolute expenses, though the expenses in the medicinal area are much lower[7].

Individuals who develop dementia before the age of 65 years are said to have early-development (or working age) dementia and those influenced after that age to have late-development dementia[7]. Changes in the progression of dementia can be decreased with lifestyle modifications like regular exercise, controlling diabetes, maintaining a healthy BMI, controlling smoking and hypertension[2]. Additionally, initially treatable dementia might become untreatable after a delay in analysis[8]. Some studies show that patients of diabetes mellitus (DM) with mild cognitive problems are prone to developing dementia in comparison to individuals that do not have diabetes with mild cognitive impairment[9]. In addition to other complications in T2DM, either microvascular or macrovascular, changes cause 1.5

to 2.5 fold increase in risk for dementia[10]. T2DM can cause early onset of dementia[11].

DM is considered as a centennial pandemic[12]. Diabetes prevalence for all age groups was estimated to be 2.8 percent by 2000 and is anticipated to rise 4.4 percent by 2030[13]. DM is a disorder of metabolism which presents as higher blood glucose levels and abnormality in the release of insulin, its effect on target tissues, or these two combinations[14]. DM is categorized into Type 1 DM, T2DM, and Gestational Diabetes. The lack of secretion of insulin causes Type 1 diabetes. People who are at risk of developing this type of diabetes can frequently be distinguished by serology of a pathologic immune system activity in the pancreatic islets, as well as genetic indicators.

In the other, considerably more prevalent class T2DM, the cause is a combination of resistance in insulin activity and insufficient insulin secretion[15,16]. Insufficient glycemic control is an important, modifiable risk factor for complications of diabetes, and the target for glycemic control should be achieved for prevention of complications[17]. Type-3-DM name has been given to dementia because of the similarity of features and association of both cognitive decline and DM[18]. Physicians believe that dementia is a contingency and ramification of DM[19]. Despite the fact that the relationship between diabetes and these mild changes in perception is currently recognized, the connection between diabetes and dementia is an area of debate.[19] Diabetes is a risk factor for dementia, yet whether anti diabetic medicine diminishes the hazard is not clear. Metformin, FDA-accepted in 1994, is an anti-diabetic drug used in T2DM. Metformin comes in both prompt release and extended release and is utilized as single or in combination with other anti-diabetic drugs[20]. Metformin has turned into the main line treatment for patients with T2DM[21]. Metformin is the anti-diabetic drug which could decreased macro-vascular complications as well as ability to control blood glucose level. Metformin is used to treat T2DM and also appears to target age related mechanisms. A few mechanisms are significant to glucose digestion, yet for aging, these may not be the most significant ones[22]. Metformin use was related with impaired cognition[23]. Some studies show decrease in the progression of dementia in metformin users of T2DM[24]. Some studies are there for targeting aging with metformin[25].

Dementia can be diagnosed by clinical findings and lab or imaging tests can give supportive evidence.[26] MMSE is the recommended analytical tool for the screening of cognition and dementia[27]. This is a relatively easy and quick to perform 30-point test and does not require additional equipment to assess the concentration, orientation, attention, naming, verbal memory, and visuospatial skills of the respondents. In our country, developing dementia is a big reason for concern. In Pakistan, insufficient data exists on the analyses and frequency of dementia in metformin users with T2DM, and their relationship to age, gender, and diabetes duration. The objective of this study is to determine association of dementia in metformin users with T2DM at JPMC Karachi. This study could help T2DM patients to identify their risk factors for dementia and seek information on how to avoid dementia or slow its progression.

METHODOLOGY

This was a cross-sectional study in which patients were recruited from the Diabetes Clinic JPMC, Karachi's outpatient department after IRB (Institutional Review Board) approval (Ref N0.f.2-81/2O2O-GENI/393228/JPMC). The study lasted six months, from February 2020 to August 2020.

Taken from previous studies, the prevalence of Dementia is 5% in most world regions[28]. The sample size was determined on the open EPI 21 version as a reference using online tools. The sample was computed as 73 patients with a margin of error of 5% and a confidence level of 95%, however, we found 83 patients with dementia out of 350 patients of T2DM.

Patients on metformin were included and all other insulin users or other hypoglycemic users were excluded. Out of 350, total 83 patients having dementia were selected by MMSE and categorized as mild dementia, moderate dementia, and sever dementia by scoring. The score of 30 is the highest in MMSE. Mild dementia is indicated by a score of 20 to 24, moderate dementia by a score of 13 to 20, and severe dementia by a score of less than 12. Patients were advised not to take any other medications except medicine of diabetic disease at least for two weeks to provide drug free interval after recruitment by MMSE. Patients were categorized as mild and moderate dementia as we did not find severe dementia. The patients were evaluated by self-generated questionnaire for association with age, gender, and duration of diabetes.

RESULTS

Table I presents that patients with mean age of 47.29±7.63 had mild dementia, whereas patients having mean age of 52.50±8.85 had moderate dementia with a p-value of 0.006 that was statistically significant. It shows that there was a strong correlation among age and the onset of dementia in T2DM. Mean duration of the years of diabetes mellitus was 3.74±2.32 in mild

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Table I: Mean Demographic Characteristics Among Mild and Moderate Dementia (n=83)

Variables	Mild Dementia Mean ± SD	Moderate Dementia Mean ± SD	p value
Age in Years	47. 29 ± 7.630	52.50 ± 8.850	0.006
Duration of DM in Years	3.74 ± 02.32	09.20 ± 3.9100	<0.0010

*Significant at p<0.05, **Highly Significant at p<0.01

Table II: Frequency of Mild and Moderate Dementia in Males and Females (n=83)

Variables Gender	Mild Dementia n (%)	Moderate Dementia n (%)	Total Dementia n (%)	p value
Male	15.(29.4%)	18.(56.2%)	33.(39.8%)	0.015
Female	36.(70.6%)	14.(43.8%)	50.(62.2%)	0.015

*Significant at p<0.05, **Highly Significant at p<0.01

dementia, while patients of moderate dementia had mean duration of diabetes 9.20±3.91 years, with a statistically significant p-value (<0.001) that showed there was strong association between dementia and the years of duration of diabetes.

Table II and Fig I show that there was a statistically significant link between gender and dementia (p-value = 0.015). Out of 83 dementia patients, men with mild dementia were 15 (29.4%), whereas 18 (56.2%) men had moderate dementia. Mild dementia affected 36 women (70.6%), while moderate dementia affected 14 (43.8%) out of 83 dementia patients. Out of 83 patients, more women (50) 62.2 % had dementia compared to men (33) 39.8%.
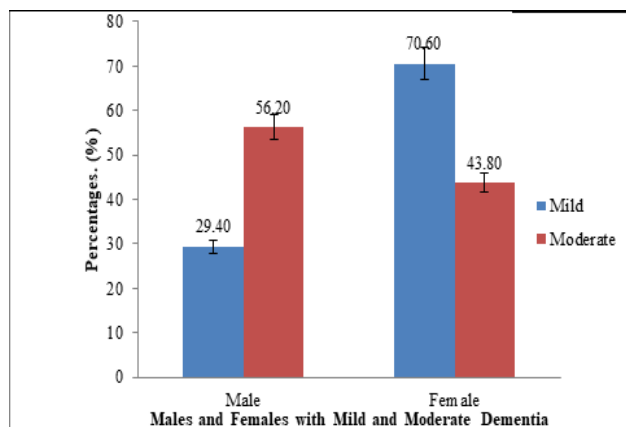

Fig. I: Frequency of Mild and Moderate Dementia Among Genders

DISCUSSION

Both dementia and diabetes are on the rise and may soon become global epidemics[28]. Diabetes and its consequences are known to raise the risk of dementia and cognitive impairment[29]. The current exploratory study aimed to look into the predisposing variables for dementia and to describe the link between T2DM and dementia in the Pakistani community.

Total 350 patients were evaluated by MMSE in which 83 dementia-affected T2DM patients were chosen for investigation, with 60.2 percent females and 39.8% males. Female patients had a greater rate of dementia among patients of T2DM than male patients with significant p-value of 0.015, which is in line with prior research[29,30]. In Pakistan, women have little awareness about the condition. Females have a greater obesity incidence and are less physically active than males, which can lead to diabetes, which can cause cognitive impairment and dementia[31].

Current study showed that the patients of mild dementia had a mean age of 47.29±7.63 while those who had moderate dementia had the mean age of 52.50±8.85 with a statistically significant p-value of 0.006 that shows strong relation among age advancement and progression from mild dementia to moderate form of dementia.

Insulin resistance in prediabetes stage has been linked to an increased risk of cognitive decline, followed by an increased risk of brain atrophic injury, which may be the cause of development of dementia[32]. Our study results show that the duration of diabetes mellitus is strongly related with the progression of level of dementia, as there was mild dementia if the duration was 3.74±2.32 years, and progress to moderate dementia when duration of diabetes in mean years was 9.20±3.91 with a highly significant value p-value (<0.001).

CONCLUSION

Findings of this study conclude that dementia in metformin users of T2DM is more in females and the risk of dementia increases with age and with the duration of diabetes.

Conflict of interest: The authors declare no conflict of interest.

Authors' Contributions: RF: Conceived the idea and reviewed the article; HA: Drafted the article and reviewed literature; SMA: Supervised and critically revised; SN: Performed analysis and editing; SSK: Reviewed and edited the draft.

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