

# Status of glycemic control among diabetic patients with dementia: experience from outpatient department of a tertiary care hospital of Bangladesh

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## ABSTRACT

**Background:** Dementia is a clinical syndrome with loss of cognitive function, thinking, remembering and reasoning. It also affects the behavioral abilities to such an extent that interfere one's daily life and activities. Alzheimer's disease is known as the most common form of dementia frequently affecting people with 65 years or more. Abnormal glycemic status carries a significant role for developing dementia in elderly individuals. The aim of this study was to assess the glycemic status of diabetic population suffering from dementia.

**Methods:** This cross-sectional study was done in the Department of Biochemistry and Molecular Biology, BIRDEM General Hospital from July 2018 to June 2019. According to inclusion criteria, after taking informed written consent from 222 respondents and their caregivers, a structured questionnaire (Addenbrooke's Cognitive Examination-ACE-III) was filled up for each subject to predict their ACE-III score. According to ACE-III score, the total study population were divided into two groups, as Group I- DM with Dementia (ACE-III score  $\leq$  70) and Group II- DM without Dementia (ACE-III score  $>$  70). Relevant biochemical parameters such as fasting and 2-hours after breakfast blood sugar and HbA1c level were measured by appropriate method. Statistical analysis was done with the help of SPSS software.

**Results:** In this study, the differences between glycemic parameters (FBS  $7.34 \pm 1.86$  mmol/L vs  $6.52 \pm 1.25$  mmol/L,  $p < 0.01$ , 2hrs ABF  $11.94 \pm 3.07$  mmol/L vs  $9.21 \pm 1.37$  mmol/L,  $p < 0.001$  and HbA1c  $8.80 \pm 2.18\%$  vs  $6.41 \pm 0.64\%$ ,  $p < 0.001$ ) between two groups were significant. A positive correlation of glycemic parameters were also found with dementia.

**Conclusion:** This study concluded that glycaemic status was poor in diabetic patients with dementia than those without dementia.

**Key words:** Vascular dementia, Alzheimer's disease, T2DM patients, HbA1c.

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## INTRODUCTION

Dementia is defined as a global impairment of cognitive function and is typically progressive and non-reversible.<sup>1</sup> Worldwide about 47 million people were in dementia in 2015 and numbers are going to predict triple by 2050.<sup>2</sup> According to the causal theory introduced by Rothman, the important causes of dementia are age, diet, diabetes, elevated homocysteine, hypertension, smoking, alcohols, physical activity, ApoE4 genotype, atherosclerosis and other vascular risk factors.<sup>3</sup> Dementia increases in prevalence with age and it is rare among people under 45 years. Genetic factors play an important role and 15% of causes are familial due to mutation of several genes.<sup>1</sup>

Diabetes mellitus is a well-established risk factor for dementia and particularly patients with type 2 diabetes

seem to have increased risk of dementia.<sup>4</sup> Geriatric syndromes especially cognitive dysfunction is emerging as a third complication category in addition to the traditional macro and micro vascular disease in older people with diabetes.<sup>5</sup> In type 1 diabetic patients, only mild to moderate mental speed and a diminished mental flexibility are evident.<sup>6</sup> But elderly type 2 diabetes patients frequently causes dementia mainly for their repeated hypoglycemic attacks, chronic hypoglycemia, glycemetic fluctuation, high LDL cholesterol and obesity.<sup>7</sup> Diabetic patients treated with metformin at a higher dose for a long period have a chance of developing dementia due to deficiency of vitamin B6 and vitamin B12 absorption, which is a cofactor for homocysteine metabolism.<sup>8</sup> Elderly diabetic patients commonly treated with anticholinergic drugs for overactive bladder have more chance of developing dementia; dementia rate was 3.9% in oxybuturin and 4.3% in solifenacin group.<sup>9</sup> In diabetes patients, hyperinsulinemia has been claimed to increased homocysteine by mutation of C677T methylene-tetrahydrofolate reductase enzyme which is an important enzyme of methionine metabolism. This could contribute to increased concentration of homocysteine in blood.<sup>10</sup> In developing countries like Pakistan, the risk for dementia in diabetic women are more compared to the men as they have less education, high obesity and less physical activities.<sup>11</sup>

According to International Diabetic Federation (IDF) Diabetic Atlas 2015,<sup>12</sup> around 425 million people living with diabetes worldwide. In Bangladesh, the number of diabetic population was about 7.1 million in 2015 which is projected to increase about 13.6 million by 2040. Some epidemiological studies show that diabetes is independently implicated in the development of dementia. As the diabetic rate in Bangladesh is very high, so dementia could be a major economic burden for our country. In a developed country, the health-care expense is about 600 billion dollars per year just for dementia. But the accurate expenses of dementia in countries like India is unknown, as most of people provide self-expenses for treatment not by the insurance claims.<sup>13</sup> Also there is no data in our country regarding any health-care expenses. Aims of this study were to assess the impact of glycemetic status among diabetic patient suffering from dementia.

## METHODS

This cross-sectional study was conducted over a period of one year from July 2018 to June 2019. A structured questionnaire (Addenbroke's Cognitive Examination-ACE-III) was filled up for each subject to predict their ACE-III score. According to ACE-III score, total respondents were divided into two groups, as Group I- DM with dementia and Group II- DM without dementia. FBS, 2-hours ABF and HbA1c were measured from all study subjects. Patients having history of recent stroke and malignancy, on psychotropic drugs, anti-thyroid medication, vitamin B6 and B12 within two months prior to the clinical assessment were excluded from this study.

### Sample collection

After overnight fasting for 8-10 hours about 4 ml of venous blood was drawn with aseptic precautions from antecubital vein from all the subjects and dispersed 2 ml in Ethylenediamine Tetra Acetic Acid (EDTA) tube for HbA1c and 2 ml was delivered in fluoride tube for estimation of fasting blood glucose. Two hours after breakfast 2 ml blood sample was collected in fluoride tube for 2-hrs after blood glucose.

### Statistical analyses

Statistical analysis were performed with the help of SPSS (23) version. Data were presented as mean  $\pm$  SD. Data were compared using appropriate statistical method like Pearson correlation test, Independent sample Kruskal-Willis test and Multiple logistic regression. Tests were considered significant at the level of  $\leq 5\%$  and considered as test of significance when  $P < 0.05$ .

## RESULTS

Total patients were 222 and most of the percipients were male with mean ACE-III total score  $67 \pm 13$  (Table I). Comparison of glycemetic parameters (FBS, 2-hrs ABF and HbA1c) of both groups were significant and that was reflected in (Table II). In this study, a positive correlation of FBS, 2-hrs ABF and HbA1c were found with dementia (Table III). This study further carried out multiple logistic regression analysis for glycemetic status influencing dementia among type 2 diabetic subjects showed in (Table IV), where found significant positive association of dementia with 2-hrs ABF and HbA<sub>1c</sub>.

**Table I.** Socio-demographic, anthropometric, clinical and biochemical characteristics of overall study population (N=222)

Variables		Frequency	Percentage
Sex	Female	86	38.7
	Male	136	61.3
Education	Primary	102	45.9
	Higher Secondary	61	27.5
	Higher Study	59	26.6
Occupation	Service	87	39.2
	Business	51	23.0
	House Wife	84	37.8
Duration of Diabetes	0-5 Years	41	18.5
	6-10 Years	118	53.2
	11-30 Years	63	28.4
		Mean±SD	
Age, years		70±6	
Body Mass Index		25.4±3.6	
ACE-III Total score		67±13	
FBG		8.9±3.4	
2Hrs After Breakfast		14.3±5.1	
HbA1c		8.5±2.2	

**Table II.** Comparison of glycemc status between groups (N=222)

Variables	Group I (n=111)	Group II (n=111)	p value
	Mean± SD	Mean± SD	
FBS(mmol/l)	7.34± 1.86	6.52± 1.25	<0.01
2hoursABF(mmol/l)	11.94± 3.07	9.21±1.37	<0.001
HbA <sub>1c</sub> (%)	8.80±2.18	6.41±0.64	<0.001

**Table III.** Correlation of dementia with different variables of interest

Variables	r	p-value
Age	0.182	0.015
Education	-0.507	0.000
BMI	0.084	0.0267
FBS	0.150	0.048
2hrs ABF	0.228	0.002
HbA <sub>1c</sub>	0.330	0.000

r, Pearson correlation coefficient\*=significant. \*p<0.05; \*\* p<0.01. \*\*\* p<0.001 Pearson correlation was used for statistical analysis.

**Table VI.** Association of dementia with different variables

Variable	Beta	p-value	95.0% Confidence Interval
Education	-0.338	0.000	-2.711, -7.94
FBS	0.046	0.299	-0.012, 0.040
2hrs ABF	0.133	0.007	0.007, 0.042
HbA <sub>1c</sub>	0.196	0.000	0.025, 0.073

Analysis was done by Multiple logistic regression.

Beta for standardized regression coefficient.

\*=significant. \*p <0.05; \* p<0.01. \*\* p<0.001. \*\*\*

## DISCUSSION

The present study showed that uncontrolled glyceamic status had significant differences between both groups with the p value of FBS was p<.01 and 2-hrs after breakfast was p<.001. HbA<sub>1c</sub> also had highly significant results with the p value <0.001. So it could be said that uncontrolled blood sugar had a great influence of developing dementia. Similar hospital based study done in Mumbai, India, accounted the proportion of dementia was more with worse glyceamic control, representing p value of HbA<sub>1c</sub> <0.05.<sup>14</sup>

Lower educational level, negligence of taking anti diabetic medication and lack of physical inactivity would be the main cause for this high proportion. Matioli et al.<sup>15</sup> also reported the same results. In present study significant positive correlation was found between dementia with Age (<0.05), BMI (p<0.05), FBG (p<0.05), 2hr AB(p<0.01) and HbA<sub>1c</sub> (p<0.001). Some previous studies also found significant positive correlation of glyceamic index in type 2 diabetic subjects.<sup>16-18</sup>

This study further carried out multiple logistic regression analysis of factors influencing dementia that showed significant differences in education and glyceamic parameters. As a low education level is related to low socioeconomic conditions and access to poor health services, it has been linked with an increased risk of dementia. Upasna et al. also reported similar results in 2017 among Indian population.<sup>19</sup> Similar results also found in western population.<sup>20</sup>

## Limitation

Although optimal care had been tried in every step of the study, there were some facts to be considered while reviewing the report as limitations of this present study.

This study was done only in one tertiary care hospital of Bangladesh, hence may not represent the whole population of the country.

## Conclusion

In conclusion, this study showed a significant association of dementia with education and glyceamic status. Among those association, education 2hrs ABF and HbA<sub>1c</sub> were reported as an independent determinant for developing dementia among type 2 diabetic patients in Bangladesh. The burden of dementia is continuously increasing and is expected to add to the socioeconomic burden mainly in countries with limited resources. In this study, worse glyceamic control had accounted a significant influence on dementia. So glyceamic control has to be proposed as a potential mechanism to reduce the prevalence of the dementia to enjoy an active retirement life.

**Authors' contribution:** HA prepared the study design, collected data, sample processing, prepared the manuscript. SMH designed the questioner, reviewed and edited the manuscript. FS helped in data collection, supervised patient management and also sample processing. SMH also performed statistical analysis and interpretation. HA also drafted and edited the research manuscript preparation, compiled data and writing. FAM supervised this study. All authors read and approve the final version for submission.

**Conflict of interest:** Nothing to declare.

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