# Evaluation of Risk Factors in Patients with Dementia

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**Abstract:**
**Background**: Dementia is a global burden. Despite recent advances, current pharmacological treatment of dementia is unrewarding. Diabetes mellitus, dyslipidemia and hypertension are being increasingly recognized as major modifiable risk factors of dementia. Therefore, an approach towards risk factor modification and neuroprotection is needed for prevention and slowing the progression of the disease. **Objective**: The objective of the study was to determine the cardiometabolic risks in patients with dementia. **Methods:** This cross sectional study was conducted in the department of Neurology of Rangpur Medical College Hospital among patients with dementia between January 2016 and December 2018. 150 eligible participants of all ages with cognitive dysfunction fulfilling the selection criteria were enrolled into the study. Mini-Mental Status Examination (MMSE) was done for each subject. All patients was undergone relevant investigations. Patients having blood glucose levels of 200 mg/dl or more at 2 hours samples were termed undiagnosed DM (UDM). The outcome variables were: age, sex, hypertension, diabetes and dyslipidemia (DL). **Results**: Out of 150 patients, 95 were males and 55 females with a male to female ratio 1.7:1. 37 subjects had known diabetes and 70 patients had unknown diabetes (detected after oral glucose tolerance test). An overall 71.33% subjects had diabetes, 65.33% had DL, 64.24% had HTN and 50% subjects had DM plus DL. The gender difference of DM (male vs female) were (64.89% vs 82.14%, p<0.02), DM plus DL (41.49% vs 64.29%, p<0.01) significantly higher in females, that of DL (60.63% vs 73.21% p=0.08)) and HTN (60.21% vs 71.42%, p=0.14) were also higher but the differences were not significant. **Conclusion**: The prevalence of diabetes among subjects of dementia was higher than dyslipidemia and hypertension. Frequency of dementia with previously unknown diabetes outweighed known diabetes and dyslipidemia. All the metabolic abnormalities were found to be worse in females suggesting a clear sex difference in dementia.

**Indexing words:** Dementia, Hypertension, Diabetes mellitus, Dyslipidemia

**Introduction:**
Dementia is an age related organic brain disorder with loss of previously acquired intellectual functions. The characteristic symptoms of dementia are difficulties with memory, language, problem-solving and other cognitive skills that affect a person's ability to perform everyday activities.[1] Genetics, higher age (>65 years) and female gender are the recognized risk factors of dementia. Trivial changes in the brain start approximately 20 years before the clinical onset of the disease with memory and language problems. Most people with dementia do not complain by themselves and brought about by relatives or friends because of dependence for survival or getting lost in a previously acquainted environment.[1] The major modifiable risk factors; insulin deficient Type 2 diabetes mellitus (DM), hypertension (HTN) and dyslipidemia (DL) may remain silent for long period until complications become overt.[2,3,4] Insulin has a neuroprotective effect[5] and a significant role in memory processing and memory preserving.[6,7] Insulin and its analogues are used successfully in treating Alzheimer's disease (AD).[8-11] Conversely, uncontrolled DM accelerate memory decline, cause dementia at an earlier age.[12,13,14] Studies demonstrate that recommended

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glycaemic targets prevent dementia and favours healthy brain aging.[15,16] An undoubted role of brain insulin deficiency or dysfunction behind the neuropathology of AD gave rise the concept of brain diabetes or "Type 3 diabetes".[17-20] This study explored the cardio-metabolic profile of patients with cognitive dysfunctions by means of levels of glycaemia, dyslipidimia and hypertension.

**Methods:**

This cross sectional study was conducted in the department of Neurology of Rangpur Medical College Hospital among patients with dementia between January 2016 and December 2018. 150 eligible persons of all ages with cognitive dysfunction fulfilling the selection criteria were enrolled into the study. Caregivers narrated the history because subjects with memory decline had inability to self care (dependence), irrelevant speech, wandering, cognitive dysfunction, loss of insight, difficulties with ADL,[21] and loss of sphincter control. Included patients were known cases of DM or unknown DM. Patients with acute organic or psychiatric illness such as confusion, delirium, stroke, myocardial injury, ongoing psychiatric treatment, insulin treated DM, alcoholic, drug addict, clinically hypo/ hyperthyroid, blind, deaf or suffering from or being treated for any obvious debilitating illness and mild dementia were excluded. Meticulous review of all previous clinical and investigation records of each patient was done to identify any relevant disease, modes of treatment and reasons that can systemically affect cognition. A detailed history, clinical examination and investigations to confirm diabetes and dyslipidemia were done. Mini-Mental Status Examination (MMSE)[22] was done for each subject and a test score of 26-30 was considered normal and score 21- 25 mild, 11-20 moderate and 10 or less was considered severe dementia. All patients were investigated for complete blood count, blood sugar, serum lipid status, electrocardiography (ECG) and brain CT/MRI to exclude organic lesion other than changes due to aging. Subjects with known or previously treated diabetes or those with a random blood sugar of more than 200 mg /dl (11.1 mmol/L)[23] on 2 or more occasions were labeled as known DM and those with normal blood sugar levels on routine tests with fasting or random samples had to undergo a standard oral glucose tolerance test (OGTT) with 75 gram glucose. After OGTT patients having blood glucose level of 200 mg/dl or more at 2 hours were termed undiagnosed DM (UDM).

**Results:**

The mean age (in years) was 61.29±13.44 (95% CI; 59.14-63) years and weight (in Kg) 57.43±10.68 (95% CI; 55.46-59.40). HTN was common with a BP (mm of Hg) systolic 155.64±24.30 (95% CI; 151.73-159.56), diastolic 94.18±12.59 (95% CI; 92.16-96.21). No sex difference was found (Table 1).

**Table 1: Distribution of patients by clinical information (n= 150)***

| Variables | Overall (n) | Males (n) | Females (n) | Student's t-test |
|---|---|---|---|---|
| Age (years) | 61.29±13.44 (150) | 62.06±14.24 (95) | 59.95±11.94 (55) | NS |
| Weight (kg) | 57.43±10.68 (113) | 59.25±9.95 (75) | 53.89±11.27 (38) | NS |
| SBP (mm of Hg) | 155.64±24.30 (150) | 153.76±23.95 (93) | 158.82±24.77 (55) | NS |
| DBP (mm of Hg) | 94.18±12.59 (150) | 93.01±13.37 (95) | 96.18±12.80 (55) | NS |

* All units were expressed as (mean ± SD). 'Students t test' was done between male and female subjects for different variables. NS= not significant.

Table 2 illustrates previously known DM in 37(24.83%) subjects and DM after OGTT in 107 (71.33%) subjects and 70 (46.67%) as unknown DM.

**Table 2: Distribution of patients by diagnosis of diabetes mellitus subjects before and after OGTT (n= 150)**

| Variable | Overall % (n) | Males % (n) | Females % (n) | Chi-squared test* |
|---|---|---|---|---|
| Diagnosed DM | 24.83 (37) | 25.80 (24) | 23.61 (13) | NS |
| DM after OGTT | 71.33 (107) | 64.89 (61) | 82.14 (46) | S 6.42/ p<0.02 |
| UDM | 46.67 (70) | 37.89 (36) | 61.82 (34) | S 8.63 / p<0.01 |

*Chi Squared test done between male and female groups. NS=not significant; S=significant at p<0.05 or less.

Fig 1 shows frequency of unknown DM outnumbered known DM among subjects with dementia.

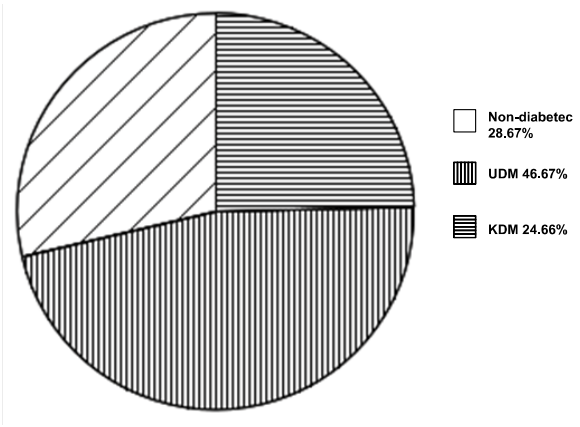



**Fig 1: Prevalence of diabetes among subject with dementia**

Fig 2 shows age distribution of the subjects with dementia. It was observed that more than 62% persons were above the age of 60 years and 28% among them were UDM.

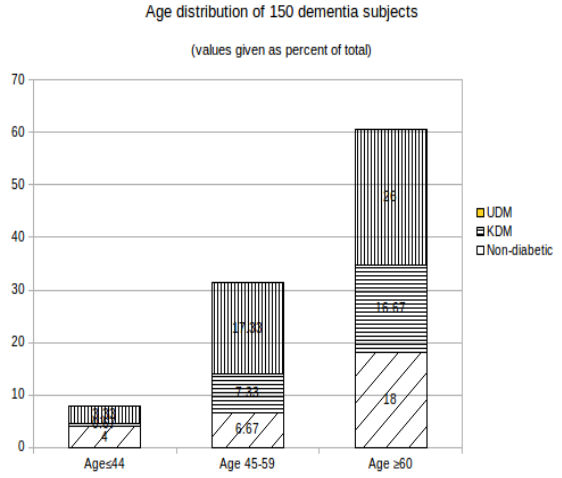



**Fig 2: Age distribution of 150 dementia subjects according to DM**

KDM=known diabetes subjects, UDM= unknown DM.

Table 3 demonstrates frequency of DM was highest (107/ 150, 71.33 %) followed by dyslipidemia (98/150, 65.33%, p<0.02).

The metabolic parameters were worse in females. The gender differences of DM (male vs female) were (64.89% vs 82.14%, p<0.02), DM plus DL (41.49% vs 64.29%, p<0.007) significantly higher in females, that of DL (60.63% vs 73.21% p=0.08)) and HTN (60.21% vs 71.42%, p=0.14) were also higher and the differences were not significant.

**Table 3:** Distribution by metabolic profile of subjects

| Problems | Overall % (n) | Males % (n) | Females % (n) | Chi Squared test* |
|---|---|---|---|---|
| DM | 71.33 (107) | 64.89 (61) | 82.14 (46) | S 6.42/ p<0.02 |
| DL | 65.33 (98) | 60.63 (57) | 73.21 (41) | NS 3.25/ p=0.07 |
| DM+DL | 50.00 (75) | 41.49 (39) | 64.29 (36) | S 8.29/ p<0.01 |

*Chi Squared test done between male and female groups. NS=not significant; S=significant at p<0.05.

**Discussion:**

Cardiometabolic risk factors increase the risk of developing cognitive impairment in the elderly population. Among the important risk factors, diabetes, hypertension and dyslipidimia are on the top of list. This study showed that 71.33 % of subjects with dementia had diabetes at the time of diagnosis, 24.83% were known DM and 46.67% had UDM. Among the participants, 65.33% had DL, 50% had DM with DL and 64.24% had HTN. Among them, DM appeared to be causally related to dementia and could be managed effectively.[24]

In this study despite higher prevalence of DM and HTN, females were found to be less susceptible to develop dementia than males. The prevalence of DL is higher in females but not statistically significant and a previous study suggests that it could be secondary to concomitant DM resulting from insulin deficiency.[25]

A meta-analysis of 28 longitudinal studies demonstrated that people with DM had a 73% increased risk of developing dementia and a 56% increased risk of developing AD compared to the general population.[26] Chatterjee et al. found 60% greater risk for the development of dementia compared with those without DM.[27] Apart from established cases of known DM, newly diagnosed diabetes was associated with a 16% increase in the risk of dementia among the elderly population.[28]

Growing evidences suggest that normal metabolic homeostasis is essential for a healthy brain and poor glycemic control over long duration leads to brain atrophy, cognitive impairment and dementia.[29,30,31,32] Insulin

deficiency or dysfunction was identified as the common etiology behind DM, DL, and HTN.[25] Subjects with cognitive impairments are frequently found to have concomitant DM.[33,34] The implication of present study findings is that people with dementia with risk factor DM can substantially improve with insulin therapy and DL, HTN can be treated adequately with appropriate therapy.[35]

**Conclusion:**

In this study the prevalence of diabetes among subjects of dementia was higher than dyslipidemia and hypertension. Frequency of dementia with previously unknown diabetes outweighed known diabetes and dyslipidemia. All the metabolic abnormalities were found to be worse in females suggesting a clear sex difference in dementia. The study concluded that cardiometabolic risk factors increase the risk of developing cognitive impairment.

**Limitations:**

This study did not include vascular or mild dementia. Greater number of subjects was hypertensive and a vascular etiology could underlie dementia in those without diabetes.

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