REPORT

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Introduction

Magnitude of type 2 diabetes mellitus (T2DM) is ever increasing in India and at present ~ 69 million people are living with diabetes [1] and another ~ 77 million people are pre-diabetic subjects, having high potential for the development of T2DM [2]. Uncontrolled serum glucose levels for extended durations are associated with retinopathy, nephropathy, neuropathy as well as cardiovascular, cerebrovascular and peripheral vascular diseases. Recently cognitive dysfunction (CD) in T2DM is gaining much attention due to their co-occurrence. Major cognitive dysfunctions associated with T2DM are psychomotor speed, executive function, verbal memory and processing speed, working memory, immediate and delayed recall, verbal fluency, visual retention and attention [3]. More than half of the brain is constituted by lipids. They play critical roles in maintaining the brain's structural and functional components [4,5,6]. Dyslipidemia and subclinical atherosclerosis are one of the major risk factors for cognitive dysfunction in T2DM patients. Several endocrine factors such as insulin resistance, thyroid dysfunction, Vitamin B 12 deficiency and use of statins also can predispose to CD in T2DM patients [7]. T2DM results into impaired neurogenesis, hyperglycemia, blood brain barrier dysfunction, inflammation, insulin resistance and vascular dysfunction.Chronically higher blood glucose levels exert a negative influence on cognition and cause structural changes in the hippocampus thereby leading to CD [8].There is a lot of heterogeneity in magnitude rates of CD in T2DM patients because of different genetic make up and dietary habits. From India, studies depicting magnitude of CD in T2DM patients are very few. The data generated may give critical inputs for the role of lipids in the occurrence of CD in T2DM patients.

Review Literature

In a French population study with 59-71 age group diabetic patients' cognitive decline was higher compared to non-diabetic individuals [11]. A study in older than 60 years of Latinos indicated that diabetes was a significant predictor for major cognitive decline [12] with 4.8% diabetic patients showing severe CD known as dementia at this age group while prevalence of CD was 31% in diabetic people aged more than 85 years [13].A systematic review of the cognitive decline in diabetes showed 1.2 to 1.5 fold increase in rate of decline in cognitive ability in diabetes compared to non-diabetic population [14]. In a Japanese elderly population study, compared to non-diabetic groups, diabetics had a significant cognitive decline, which was well correlated with hippocampal atrophy but not whole brain atrophy [15]. In a Croatian study on adult population diabetics had higher cognitive dysfunction compared to controls [16]. In an US study, diabetes was associated with cognitive decline (1.39 fold) in elderly person above 70 years of age [17]. In a Polish study, 31.5% diabetics had CD, the age group was above 65 years [18]. In a Taiwanese study with an age group of 65 or above, 11.5% of the diabetic population had CD compared to control population [19]. In a Chinese large cross sectional study 13.5% of the diabetic population above 65 years of age had mild cognitive dysfunction [20].In an Australian adult population study, cognitive decline was associated with impaired cerebrovascular responsiveness in T2D [21]. In a Greece population study of diabetic patients above 65 years of age, 2 fold higher chances of CD was observed compared to control population [22]. A study in Punjab stated 33.73% diabetic population suffering from cognitive impairment while the remaining 66.27% were found to have normal cognitive function. The higher prevalence rate of cognitive impairment was found in women with diabetes and majority of these patients remained undiagnosed for it. But studies are lacking from other parts of the country which we believe will change the magnitude rate due to the variation in genetic make up and dietary intake. So future studies are required in this field for better management of the disease.

Objectives

- **To measure the magnitude of cognitive dysfunction in T2DM patients (completed) [note: instructed to collect more by DAC members]**
- To compare serum targeted lipidomics in T2DM patients with and without cognitive dysfunction

- Identifying key lipid molecules altered in cognitive dysfunction in type 2 diabetes mellitus for future studies

Methodology

The study was conducted after Institutional Ethics committee approval. This study is a cross sectional observational study conducted at General Medicine Department, Kasturba Hospital Manipal.1300 T2DM patients were recruited for this study. Our main objective was to measure the magnitude of cognitive dysfunction in type 2 diabetes mellitus patients. Demographic data and medications prescribed to all the T2DM patients visiting to Medicine OPD, Kasturba Hospital Manipal above 20 years of age who volunteered and co-operated for the study were noted. Montreal Cognitive test and Digit Symbol Substitution tests were conducted to assess cognitive abilities in all T2DM patients with informed consent. Patients having all the co-morbidities like hypo and hyperthyroidism, hypertension, CAD, kidney and liver diseases, HIV, Vitamin B12 deficiency and any other infectious diseases and minimum of 5 years of formal education were included for this study whereas patients who were severely sick, with visual impairment, confusion, delirium and un co-operative for performing the cognitive tests were excluded from the study.

Results of the work progressed so far

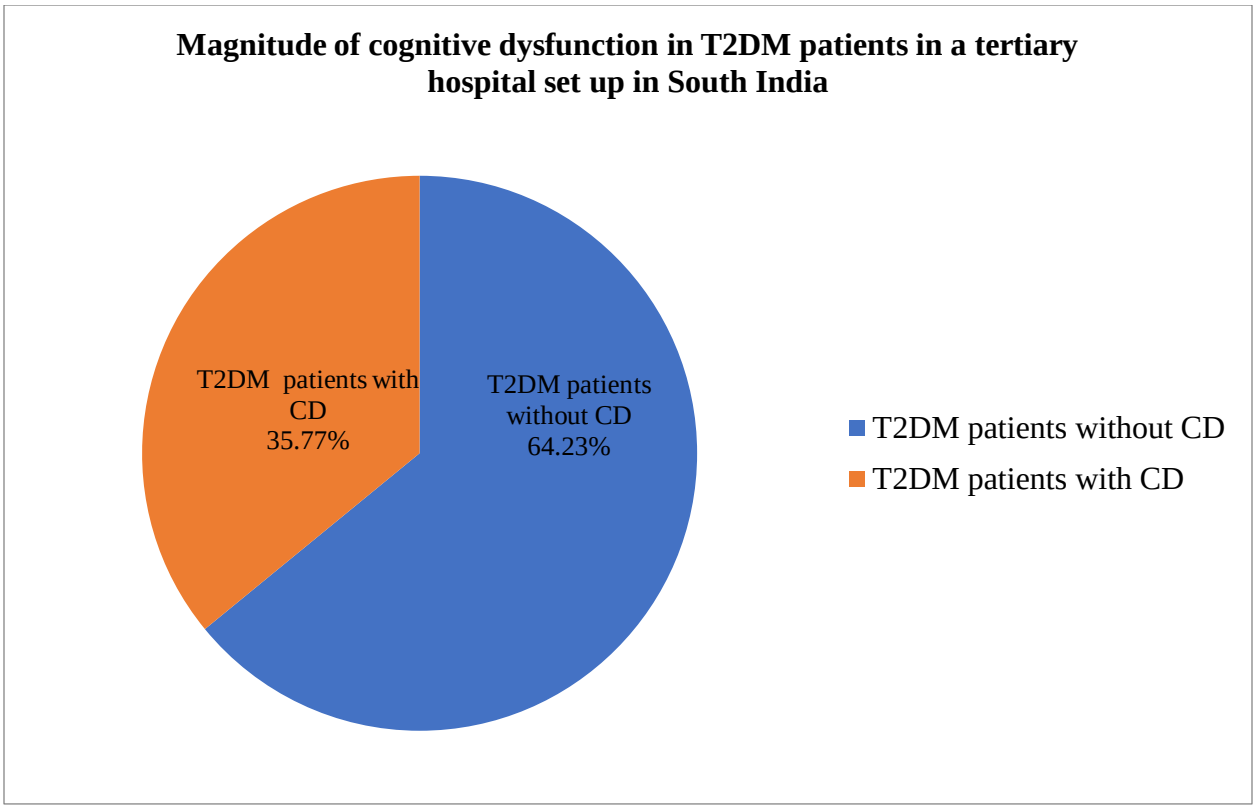

Figure 1: **Pie diagram**: Out of 1300 T2DM patients recruited for this study 64.23% of them had proper cognitive function whereas the remaining 35.77% had cognitive dysfunction

Table 1: Comparison between clinical variables and baseline characteristics in T2DM patients with and without CD (Independent Samples t test)

Name of the variables	**T2DM patients without CD** **Mean ± SD (n=835)** **Median (Q1,Q3)**	**T2DM patients with CD** **Mean ± SD (n=465)** **Median (Q1, Q3)**	P value
Age (years)	55.62 ± 10.61	62.21± 10.29	.256
Height (cm)	163.41 ± 9.32	159.42 ± 8.25	.179
Weight (Kg)	68.93 ± 12.3	64.76 ± 12.04	.692
BMI (Kg/m^2)	25.67 ± 4.68	25.51 ± 4.52	.521
TC (mg/dl)	165.34 ± 45.78	166.49 ± 46.86	.892
HDL (mg/dl)	40.63 ± 12.28	42.24 ± 12.45	.258
LDL (mg/dl)	92.95 ± 38.88	94.24 ± 39.79	.758
Non HDL (mg/dl)	124.71± 44.06	124.24 ± 45.80	.615

<u>Table 2</u>: Comparison between clinical variables and baseline characteristics in T2DM patients with and without CD (Mann Whitney test)

Name of the parameters	T2DM patients without CD Median (Q_1,Q_3) (n=835)	T2DM patients with CD Median (Q_1,Q_3) (n=465)	P value
FBS (mg/dl)	139 (117,178)	141 (116, 185)	.633
PPBS (mg/dl)	204 (161,268)	210 (167,287)	.054
Glycated Hb (mg/dl)	7.5 (6.7, 9)	7.9 (6.85, 9.2)	.010*
DSST	41 (31,51)	17 (13,23)	<.0001*
LDL/HDL	3.03 (2.32,1.59)	2.23 (1.53, 3.06)	.385
TC/HDL	4.08 (3.25, 5.11)	3.85 (3.11,5)	.063
VLDL (mg/dl)	25.8 (19.4,35.8)	27.6 (20.5,38.8)	.029*
TG (mg/dl)	138 (103,194)	149 (122,182.5)	.029*