

Impact of Cognitive Deficits on Health Related Quality of Life and Everyday Functioning in Middle Aged Type 2 Diabetes Mellitus Patients

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Type 2 diabetes mellitus (T2DM) is considered a common metabolic disorder, which is characterized by chronic hyperglycemic episodes, insulin resistance and relative insulin deficiency [1,2]. Although in the past it was considered a disease primarily of the elderly population, today's unhealthy lifestyle has shifted the disease to younger age groups, particularly middle aged adults, with significant implications on their physical, mental and cognitive health status and overall quality of life. Common physical complications include nephropathy, retinopathy, and cardiovascular disorders [1,2]. On the other hand cognitive deficits, especially in new learning - episodic memory, information processing speed and executive functions are frequent, and may influence everyday functioning capacity and employment status in salary earning middle aged adults [1,4,7]. Cognitively impaired (T2DM) patients also have a higher relative risk for developing mild cognitive impairment and accelerated progress to dementia compared to healthy adults [6,8]. Although the exact cognitive mechanisms underlying cognitive impairment in (T2DM) have not been fully established, advanced neuroimaging techniques, such as functional-MRI and diffusion MRI have detected microstructural lesions in the cerebral gray and white matter of these patients that affect structural and functional connectivity [3].

It is generally accepted in the literature that (T2DM) may negatively influence health related quality of life, activities of daily living and employment status in this population [9-11]. A study by Prassana Kumar HR., *et al.* [12] reported that the most affected domain was the restriction of their diabetic patients regarding their meals. Moreover, a cross-sectional survey found that mortality rate, complications associated with (T2DM), longer duration of diabetes and poorer general health were independent risk factors for quality of life among their diabetic patients [9]. In a more recent study [11] noted that their diabetic patients' global health related quality of life (HRQOL) was negatively influenced by older age, female gender, occupation status, various comorbidities, and the duration of diabetes. In an interesting study [7] reported that undiagnosed cognitive dysfunction in their type 2 diabetics was associated with a poorer health status. The authors suggested that diabetic patients with cognitive impairment are a vulnerable patient group who may benefit from treatment and care tailored to their special needs. Furthermore, a study by Ojo O and Brooke JE [13] noted that diabetes self-management is significantly affected by cognitive impairment, highlighting the need for detecting cognitive deficits as early on in the disease progress as possible, in order to apply structured education and behavioural strategies, which may lead to required lifestyle changes.

Although cognitive impairment in type 2 diabetics has been clearly identified, there remains a major concern regarding its treatment. The most recent Cochrane review [14], which evaluated the efficacy of various treatment options regarding cognitive dysfunction, found relatively poor evidence that any specific treatment or strategy can prevent or delay cognitive impairment in this population. It concluded that only intensive and standard glycemic control provided moderate evidence regarding their efficacy on cognitive functioning over a period of 40 to 60 months.

Another issue that becomes evident on reviewing the literature exploring cognitive dysfunction and the associated health related quality of life in type 2 diabetics is the absence of empirical studies. Furthermore, in the scarce studies that do exist, the samples of type 2 diabetics are older aged adults or elderly patients, and there is a scarcity of studies investigating samples of middle aged adult's, younger than 60 years old. In light of the above, we investigated the impact that cognitive deficits may have on the health related quality of life, employment status and everyday functioning capacity in middle aged patients diagnosed with type 2 diabetes mellitus.

We recruited forty-four patients diagnosed with T2DM and 28 healthy middle aged adults from the outpatient endocrinology units of the Laiko Hospital in Athens, and from the University General Hospital of Patras, Greece. All participants were included after having been diagnosed with T2DM by an experienced diabetes specialist according to internationally recognized criteria [1]. The research protocol was approved by the Ethics Committee of both institutions. Our patients and healthy participants were on average under 60 years old and did not differ significantly regarding demographic characteristics (age, education, general mental state, estimated premorbid intelligence levels). Diabetic patients had a mean disease duration of 6.5 years, BMI of 30.08, glycosylated haemoglobin levels (HbA1C) of 8.78, and had an average of 4.90 hypoglycaemic episodes per month. All participants were assessed with a comprehensive battery of neuropsychological tests sensitive to cognitive deficits in diabetic patients and standardized for the Greek population (Mini Mental State Examination (MMSE), Wechsler Abbreviated Scale of Intelligence (WASI), the Rey Auditory Verbal Learning Test (RAVLT), Greek verbal fluency task, Symbol Digit Modalities Test (SDMT), Trail Making Test (TMT), part A and part B) [15-25]. Mood was evaluated with the Beck Depression Inventory - Fast Screen [26] and health related quality of life with the WHOQOL-BREF self-report questionnaire [27,28].

Our results indicated that glycosylated haemoglobin levels (HbA1C) and an interaction of age, education and premorbid intelligence were the most significant predictors of cognitive performance in our middle aged diabetic sample. Moreover, by dividing our diabetic patients into two subgroups, based on their different levels of cognitive performance (i.e. the diabetic group with normal cognition performed up to 0.5 SD below the healthy group or normative data for each measure and the diabetic group with impaired cognition consisted of patients who performed at least ≤ 1.5 SD below the normative data or healthy group for each utilized measure). We found that 61.90% of our patients had impaired episodic memory, and significant differences were found on the WHOQOL-BREF questionnaire in the domains of "psychological health" [$t(40) = 2.502, p = .017$] and "environmental health" [$t(40) = 2.643, p = .012$], based on RAVLT total verbal memory learning score, with the cognitively impaired diabetic group showing poorer HRQOL on both the previously mentioned domains. Furthermore, (73.80%), of our patients had impaired executive function, and comparisons between the two subgroups' performance on WHOQOL-BREF based on the TMT-part B, demonstrated statistically significant differences between the two groups on the "social relationship" [$t(40) = 2.557, p = .014$], and "general health" domains [$t(40) = 2.773, p = .009$], with the cognitively impaired diabetic patients performing poorer in both QOL domains. On the other hand, we found that employed diabetic patients performed significantly better on measures of executive function (cognitive flexibility) compared to non-employed patients.

Our findings have significant implications in terms of everyday functioning ability and health related quality of life in middle aged type 2 diabetics. In this respect, even mild to moderate deficits on episodic memory and executive functions may negatively impact diabetes self-management behaviors, such as insulin adjustment skills and reduced self-care activities [29]. Furthermore, diabetic patients with episodic memory difficulties may have difficulty acquiring new information and skills, and possibly have a higher forgetting rate, with associated negative feelings, lower self-esteem, and reduced opportunities for leisure activities. On the other hand diabetics with executive dysfunction may become less cognitively flexible, have difficulties planning, organizing and completing everyday mentally demanding,

effortful tasks or with their interpersonal and social relationships, and difficulties in retaining their employment leading to overall reduced quality of life. From this perspective, it is extremely important that research efforts continue to clarify the clinical significance and implications of cognitive impairment for everyday functioning ability and quality of life in this population.

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