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COGNITIVE QUALITY OF LIFE IN DIABETES MELLITUS-IMPLICATION FOR COGNITIVE ASSESSMENT AND REHABILITATION

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Abstract

Diabetes Mellitus (DM) is a diagnostic term for a collection of disorders which, among other features, have in common chronic elevation of blood glucose (BG) concentration commonly referred to as hyperglycemia. Diabetes is a result of the body's inability to effectively control usage and storage of the body's main source of fuel (glucose).It is the leading cause of foot amputations, kidney failure, and blindness and is a major contributor to cardiovascular complications, such as heart attacks.
Diabetes Mellitus is a complex metabolic disease that can have devastating effects on multiple organs in the body. Diabetes is the leading cause of end stage renal disease and is also a common cause of vision loss, neuropathy, and cardiovascular disease. A less addressed and not as well recognized complication of diabetes is cognitive dysfunction. Patients with type 1 and type 2 diabetes mellitus have been found to have cognitive deficits that can be attributed to their disease. Both hypoglycemia and hyperglycemia have been implicated as causes of cognitive dysfunction, and many patients fear that recurrent hypoglycemia will impair their memory over time. Although much research has been done, the pathophysiology underlying this complication is not well understood, and the most appropriate methods to diagnose, treat, and prevent cognitive dysfunction in diabetes have not yet been defined. In addition, it should be noted that the field of cognitive dysfunction in diabetes is still in its early stages. There is a strong evidence supporting significant association between diabetes and cognitive dysfunctions, established through many hypotheses. The causative mechanism involved in such associations is only implied and still need to be investigated. This presentation highlights the need for cognitive assessment in the diabetic stages and also the requirement of rehabilitative process to maintain and enhance cognitive quality of life in diabetic care.

Key words: *Cognitive Assessment, Cognitive deficits and Diabetes Mellitus.*

INTRODUCTION

Different theoretical models of health and disease are proposed by health researchers. The emergence of interactive model of mind and body has significantly contributed for understanding the concept of health and its promotion. Modern Health psychologists have been successfully applying the 'Biopsychosocial Model' in dealing with major health issues in the community. Another important clarity that emerges from this model is the impact of the disease on the psychological and social aspects and also overall Quality of life. Health models thus explain not only the onset of disease, its management, progress of disease. But they also explain its impact at different level substantiating the multidimensionality, multifaceted component of health.

Lifestyle factors such as smoking, alcohol intake, stress, food habits, lack of exercise and sleep disturbances contributing to several non - communicable diseases is clearly documented. On the other hand disease affecting the life activities ,life processes, quality of life need to be documented for the purpose, promotion, management and rehabilitation of Coronary Artery Disease (CAD), Diabetes Mellitus ,Cancer, Stroke and Hypertension. These diseases fundamentally affects the organ, specific functions and process, is a threat to life of the individual and on the same note it affects the cognitive, psychological and emotional functioning of the individual which impact their quality of life and also contributes to its deterioration.

DIABETES MELLITUS

Diabetes is the third most common chronic disease and one of the leading causes of death [Centers for

disease control and prevention, 2013]. Diabetes is defined as a chronic condition of impaired carbohydrate, protein and fat metabolism that results from insufficient secretion of insulin or from insulin resistance". Type II diabetes or non insulin dependent results from insulin resistance, even though insulin is present in the body. The cell develops resistance to insulin. Insulin is the hormone secreted by beta cells of the pancreas, that bonds to the receptor sites on the outside of the cell and acts essentially as a key to permit glucose to enter in to the cells. Since insulin resistance is developed ,the glucose stays in the blood instead of entering the cells, resulting in a condition called "Hyperglycemia".

The body attempts to rid itself of this excess glucose, yet the cells are not receiving the glucose they need and send messages to the hypothalamus signaling that more food is needed. Glucose metabolism involves a delicate balance between insulin production and responsiveness. As food is digested, carbohydrates are broken down in to glucose. Glucose is absorbed from the intestine in to the blood, where it travels to the liver and other organs. Rising level of glucose in the blood trigger the pancreas to secrete insulin in to the blood stream. When this balance goes awry, it sets the stage for Type II diabetes. First cells in muscle, fat and liver lose some of their ability to respond fully to insulin ,a condition known as 'Insulin Resistance'. The pancreas temporarily increases its production of insulin. At this point, insulin producing cells may give up with the result that insulin production falls and the balance between the action and insulin secretion become deregulated, resulting in Type II diabetes .

INCIDENCE AND PREVALENCE

World health organization (W.H.O) report estimates that in India nearly 50 million people are diagnosed of Type II diabetes [International Diabetes Federation,2014]. Nearly 6.3 percent of world population has diabetes and roughly 5.2 million cases remain undiagnosed [American Diabetes Association, 2000].The incidence cases of Type II diabetes is increasing so rapidly that it is considered a Pandemic [Taylor,2004]. World health organization (W.H.O) has projected that the global prevalence of Type II diabetes will be more than double form 135 millions in 1995 to 3000 million by 2025. In past 40 years, the incidence of diabetes has increased six fold and each year physicians diagnose nearly 1.3 million new cases [American Diabetes Association,2012].

MANAGEMENT

Management of diabetes includes pharmacological intervention by means of oral hypoglycemic drugs and by intake of insulin to reduce the glucose level in the blood stream. Other aspects of management includes life style and behavioral changes, to prevent further complications associated with diabetes, which includes adherence to treatment regimens like diet, exercise, monitoring blood sugar levels, involving in physical activity ,to cope up stressful events and to engage in positive health behaviors. One of the major issues relevant to management in quality of life of individual in relevant to their clinical status and intervention. More specifically the functionality, productivity which to a large extent involve cognitive processes.

COGNITIVE DYSFUNCTION IN PATIENTS WITH DIABETES

Cognitive dysfunction in patients with diabetes mellitus was first noted in 1922, when patients with diabetes, who were "free from acidosis but usually not sugar free," were noted to have impaired memory and attention on cognitive testing compared with controls. Since then, there have been many studies designed to better delineate the scope and magnitude of cognitive dysfunction in diabetes. A substantial body of research into diabetes has examined the effects of the illness on cognitive functioning.

Research findings by Marzieh Nazaribadie, Masoud Amini, Mohammad Ahmadpanah, Karim Asgari, Somaye Jamlipaghale & Sara Nazaribadie (2014) suggest that diabetic patients experience decline in executive functioning and thus, monitoring neuropsychological status besides controlling levels of blood sugar in these patients is important. Studies by Yates Sweat, Yau Turchiano & Convit A (2013) states that, chronic hyperglycemia and associated micro vascular disease appear to be the most important determinants of cognitive decrements in diabetes. among well-functioning older adults, Diabetes Mellitus and poor glucose control were associated with worse cognitive function and greater decline and that suggested that severity of Diabetes Mellitus may contribute to accelerated cognitive aging,(Van Simon sick, Suzanne Satterfield, Jane A. Caule , Caterina Rosano, Elsa Strotmeyer & Tamara Harris,2012). Type 2 diabetes is associated with cognitive deficits, although inconsistently across neuropsychological domains. It is clinically and theoretically important to examine sequential change in multiple domains over time, stated by, Fischer AL, Yeung SE& Dixon RA (2012).

Shuba N & Karan (2012) in their research findings states that, Diabetes is associated with lower levels of the cognitive function. By the early implementation of Mini Mental Status Examination, even a mild cognitive impairment can be detected, so that adequate treatment can be given, to prevent dementia. A new study by Anahad O' Connor (2012) adds to growing evidence that the complications of diabetes may extend to the brain,

causing declines in memory, attention and other cognitive skills.

PATHOPHYSIOLOGY OF COGNITIVE DYSFUNCTION IN DIABETES MELLITUS

The cognitive dysfunction or impairment involves disturbances in thinking ability, memory, problem solving and decision making process. The impaired cognitive function have an effect on routine activities which indirectly lowers the quality of life among individuals, afflicted by various diseases.

The pathophysiology underlying the development of cognitive dysfunction in patients with diabetes has not been completely elucidated. Many hypotheses with supporting evidence exist, including potential causative roles for hyperglycemia, vascular disease, hypoglycemia, insulin resistance, and amyloid deposition; it may be that the cause of cognitive dysfunction in patients with diabetes will turn out to be a combination of these factors, depending on the patient's type of diabetes, co-morbidities, age, and type of therapy. A brief outline of the implication of each of these factor is examined to understand its role in influencing cognitive processes.

THE ROLE OF HYPOGLYCEMIA

Mild to moderate levels of hypoglycemia commonly affect higher-order cognitive functions. Patients may experience mood changes and difficulty with memory, planning, attention and concentration. Mental speed rapidly decreases, while accuracy remains relatively unaffected. With severe hypoglycemia, all cognitive functions may be affected, seriously decreasing a patient's mental capabilities, according to Chris Moran & Velandai Srikanth (2013). Whereas blood glucose can be quickly restored, cognitive dysfunction may take up to 4 hours or more to recover fully. Acute effects of hypoglycemia on brain structure in diabetes are rarely reported and pre-clinical data suggest that brain damage after hypoglycemia may be the result of reactive hyperglycemia through overcompensation of counter-regulatory actions.

Hyperglycemia appears to be related to abnormalities in cognitive function in patients with both type 1 and type 2 diabetes. However, the mechanisms through which hyperglycemia might mediate this effect are less than clear. The acute effect of hyperglycemia on cognition seems relatively mild, contrary to the long-term effects, and may be associated with diabetic ketoacidosis. Research findings of Yates Sweat, Yau Turchiano & Convit A (2013) states that hyperglycemia may affect cognitive function by altering synaptic plasticity in the brain, increasing levels of oxidative stress, and/or subtly altering the cerebral microvasculature. It is suggested that treatment of diabetes may lead to slight or occasionally more severe periods of hypoglycemia, which may translate to structural and metabolic alterations of the central nervous systems and subsequent cognitive dysfunction. However, it has been observed by Nine year study by Kristine Yaffe, Cherie Falvey, Nathan Hamilton, Ann V. Schwartz, Eleanor Simonsick, Suzanne Satterfield, Jane A. Caule, Caterina Rosano, Elsa Strotmeyer & Tamara Harris (2012) that subtle diabetes-related cognitive changes are associated with chronic hyperglycemia rather than episodes of hypoglycemia. Thus the chroncity of hypo and hyper glycaemia is implicated in the cognitive dysfunction due to its impact on brain structures and neural process.

THE ROLE OF VASCULAR DISEASE

Patients with diabetes have a 2- to 6-fold increased risk in thrombotic stroke and vascular disease has long been hypothesized to contribute to abnormalities in cognition in such patients. Research by Berit Inkster & Brian M Frier (2012) found that patients with diabetes have also been found to have decreased global rates of cerebral blood flow as measured using xenon, and the magnitude of reduction correlates with the duration of the disease. Interestingly the rate of cerebral blood flow in patients with diabetes is similar to that found in Alzheimer's patients with dementia. One can speculate that the decrease in cerebral blood flow, coupled with the stimulation of the thromboxane A2 receptor known to occur in patients with diabetes, could contribute to the inability of cerebral vessels to adequately vasodilate, which may in turn increase the likelihood of ischemia, according to the research findings of Anahad O' Connor (2012).

THE ROLE OF INSULIN RESISTANCE AND AMYLOID

Mild cognitive impairment is associated not only with age of diabetes onset and disease duration but also with insulin treatment. The risk of dementia is also highest in people with diabetes treated with insulin. Hyper insulinemia in non diabetic individuals has also been associated with cognitive impairment, (Alencar RC, Cobas RA, & Gomes MB (2010). This association is confounded by other co morbid factors, disease duration, and disease severity. However, there is several sound biological mechanisms by which prolonged hyper insulinemia may influence central nervous system function. Not only is insulin a vaso active substance, but it also inhibits "housekeeping" processes important for healthy brain aging (i.e., autophagy) and influences processing of proteins related to Alzheimer disease. Prolonged exposure of the brain to higher than physiological levels of insulin may alter metabolic pathways in a manner that is deleterious to cognitive circuitry, given that this circuitry is dependent on cells influenced by these metabolic processes. These factors likely impact the changes associated with the

phenomenon of “brain insulin resistance” observed in Alzheimer disease, (Astrid Nooyens, Caroline Baan, Annemieke M.,W. Spijkerman, & Monique Verschuren, (2010)

Neural networks have been shown to be acutely altered by structural lesions causing cognitive deficits and are altered in at-risk populations prior to structural changes such as atrophy before clinically measurable effects on cognition. Therefore, measures of neural networks may be best suited to track the earliest effects of diabetes on brain function. “Chronic hyperglycemia, among other factors, may negatively affect brain functioning even before micro vascular damage becomes manifest.”Metabolic a very complex organ, housed in our skull, which is made up of a number of different areas, Frontal lobe is responsible for thought, learning and behavior, Parietal lobe is responsible for processing sensory experiences and understanding, Temporal lobe is responsible for memory and certain emotions ,Occipital lobe is responsible for processing visual information, Cerebellum: responsible for coordination of movement derangements associated with chronic exposure to either hyperglycemia and/or hyper insulinemia may be more prominent in the development of diabetes-associated cognitive decline.

The brain is, balance and some reflex actions and Brain stem is responsible for regulating breathing, heart rate, blood pressure and body temperature. The skull helps to protect us from external blows which could damage brain cells. The blood-brain barrier is a membrane which protects the brain from any harmful pathogens that may be present in the blood. The brain requires nutrients, however, such as oxygen and glucose, so the blood-brain plays an important role in enabling good nutrients in and keeping harmful cells away.

The other contributors for cognitive impairment is not only the presence of diseased condition, but also due to the management procedures in the diseased conditions. For example drugs, surgical procedures, morbidity status, restriction on diet etc. Further the impaired cognitive functions can also affect the moods and emotions and the moods and emotions may produce cognitive impairment. Due to the interrelated aspects of these functions, the patients experience more stress and the quality of life deteriorates, (Jennifer Amy & Lindsan Friesen,2014) The major affective factor present in diabetes mellitus is depression which can influence cognitive performance. The focus of holistic management and rehabilitation is to address all the psychological components of individuals.

IMPORTANCE AND RELEVANCE OF COGNITIVE QUALITY OF LIFE

Cognitive functions are important for daily activity, mobility, physical activity and social activity. Impaired cognitive functions interfere with self care, basic occupational performance, communication, well being, personal and inter personal relationships, thoughts, life events and global emotional functions. It also interferes with sleeping patterns, eating, alertness and emotional behaviors. Among the clinical groups, cognitive quality of life plays a major role in determining quality of life by facilitating return to normal life, which in turn is related to work life adjustments. These cognitive functions are multidimensional, which are essential for daily living. Ability to live independently, take care of self, economic and emotional independence, interpersonal adjustment and also successful rehabilitative process is to a large extent determined by cognitive quality of life.

MODALITIES FOR ASSESSMENT OF COGNITIVE DYSFUNCTION IN PATIENTS WITH DIABETES MELLITUS

The domains of cognitive functions are so vast and complex and the process of assessing and detecting the neuro cognitive function has made it difficult to clearly demark the cognitive dysfunction associated with diabetes mellitus. Neuro cognitive testing in which an examiner administers a battery of tests to assess different aspects of cerebral function has long been the gold standard for the assessment of neuro cognitive function. Although cumbersome to administer and score, it has been very useful in assessing neuro cognition in a variety of disease states, including diabetes. However, such tests have a relatively high rate of intra subject variability that reduces their ability to identify mild deficits in preclinical disease status. Also, many studies examining the effect of diabetes on brain function use multiple neuro cognitive tests that assess the same psychological process. When the results of these different tests don’t agree, determining which results to base conclusions on can be confusing.

In addition, not all neuro cognitive tests are created equal. Although many neuro cognitive tests are well validated in a diverse population to distinguish between “normal” and “abnormal” results, other tests do not have adequate reliability data, are based on unacceptably small norms, are administered inappropriately, or do not properly distinguish between two or more diagnostic groups. Finally, neuro cognitive testing is unable to provide specific information about the neural structures responsible for any dysfunction identified. For example, although it appears that white matter function such as processing speed, attention, and visual-spatial processing are particularly affected by diabetes, localization of this dysfunction to white or gray matter is not possible using the battery of tests available to assess neuro cognition.

Because of the limitations in neuro cognitive testing, a number of modalities have been used to assess cognitive function in patients with diabetes. One of the oldest modalities has been to measure electrical activity

such as evoked response potentials in the brain after the administration of different stimuli. Abnormal evoked response potentials can reveal subclinical sensory nerve conduction deficits that may not otherwise be apparent. Increased HbA1c was related to reduce cognitive performance,(Yaffe Grodstein, Croxson,Jagger Davis Cohen & Colombo Simolke, 2012). Event-related potentials have also helped define brain adaptations to hypoglycemia,(Manjeet Singh, Naresh Kumar, Sushma Sood, Renu Garg, Uma Garg & Jeewandeep Kaur1 ,2013).

Research by Fischer AL, Yeung SE, & Dixon RA (2012) states that in patients with type 2 diabetes, white matter hyper intensities have been noted to correlate with reduced performance on tests of attention, executive function, information processing speed, and memory. The nature of these white matter lesions is uncertain, but investigators have hypothesized that they could represent demyelination, increased water content, angionecrosis, cystic infarcts, or gliosis (i.e. brain tissue scarring).MRI has also demonstrated that subjects with type 2 diabetes have hippocampus and amygdala atrophy relative to control subjects. Functional MRI (fMRI) has also been used to assess cerebral function in patients with diabetes. fMRI is based on the fact that increases in cerebral blood flow and metabolism during stimulus-induced neuronal activation are accompanied by a relative reduction in deoxyhemoglobin content of the activated tissue relative to the adjacent inactivated brain. Other imaging modalities such as single photon emission computed tomography (SPECT) and PET have been used to assess cerebral function in patients with diabetes mellitus, (Virginia Elderkin-Thompson, Gerhard Hellemann, Rakesh K. Gupta, & Anand Kumar,2009). These evidence warrants a need to clarify the status of cognitive performance among diabetic patients across the treatment phases to maintain the cognitive quality of life and also to take up appropriate steps to restore the functions.

ROLE OF INTERVENTIONS TO ENHANCE COGNITIVE FUNCTION IN DIABETES MELLITUS

Intervention can be defined as “Any attempt to intervene the usual sequence in the development of disease”. And also means to promote health and well being”. Various studies states that the combination of cognitive behavioral therapy and supportive diabetes education is an effective non pharmacological treatment in handling emotional issues particularly depression in patients with Type II diabetes. It may also be associated with improved glycemic control. A variety of cognitive behavioral interventions have been under taken with diabetes to improve adherence to aspects of their treatment regimens . Research has also shown the efficacy of a number of psychosocial therapies that can improve regimen adherence, glycemic control, psychosocial functioning, and quality of life. More research in this area is needed to develop psychosocial intervention programs for specific patient populations and to demonstrate the cost-effectiveness of these approaches.

Carla Ruis, Geert Jan Biessels,Kees Gorter, Maureen van den Donk,Jaap Kappelle, and Guy Rutten, (2009) in their study summarized that cognitive decrements can be found in the early stages of type 2 diabetes. This finding may have implications for diabetes education and self-management behavior in diabetic patients. Diabetes educators should at least take into account the immediate memory and learning rate and the incidental memory of patients with a recent diagnosis of diabetes. If one wishes to prevent diabetes-associated cognitive decrements, interventions may need to be initiated at a very early stage. Further they concluded that offering a smoking cessation consultation would be the best option in those patients who are smokers. Research by Anto Madison Delamater, Jacobson, Anderson, Cox, Fisher, Lustman, Rubin & Wysocki (2001) demonstrated that psychosocial factors play an integral role in the management of diabetes in both children and adults.

However, the need to enhance cognitive quality of life of patients through specific interventions like physical exercise, cognitive training and medical treatment is sporadically studied. This dimension of rehabilitative process is yet to be initiated to incorporate them as a holistic management of long term consequences.

CONCLUSION

There is an increased burden of non-communicable disease in community with prevalence of Coronary artery disease and Diabetes escalating. The burden is more felt in relation to health cost and production lost. The main stream of medications focus on disease management through medical interventions, disease prevention through risk factors reduction. The biomedical end points like reduction in atherosclerosis, coagulation and cardiac events and reduction in blood sugar and blood pressure are the main focus in medical management. Studies have revealed cognitive, psychological and social impact of the disease which affect the quality of life. Psychological intervention has focused on stress management, emotional management and primary social support to enhance better prognosis. Although much research has been done on the impact of diabetes mellitus on cognitive function, many questions still remain. It is clear that patients with type 1 and type 2 diabetes have been found to have abnormalities in neurocognitive function, although the natural history and clinical significance of these findings have not yet been clearly defined.

In prior decades, this was not an issue because patients with type 1 diabetes died at relatively young ages from other complications of the disease. However, now that patients with type 1 diabetes are living longer and better with the disease, this must be assessed. Finally, it is not clear whether the subtle cognitive deficits

identified in many studies truly impact the lives of patients living with diabetes. Future studies, perhaps longitudinal in nature or involving better serum/imaging biomarkers, will be of tremendous benefit in providing better understanding of the natural history of this complication. Although it seems that hyperglycemia and hyperglycemia-induced end organ damage contribute to this problem, the actual mechanisms through which hyperglycemia alters cerebral structure and function are not clear. Improved glycemic control is likely of therapeutic benefit, as has been suggested by many retrospective studies, but a prospective study is needed to determine whether this is true and to establish whether cognitive impairment is reversible. In addition, identification of the mechanisms through which hyperglycemia may impair cognitive function in patients with diabetes will stimulate new research into ways to prevent and treat all of the hyperglycemia-associated complications of diabetes.

The deleterious effects of diabetes mellitus on the retinal, renal, cardiovascular, and peripheral nervous systems are widely acknowledged. Less attention has been given to the effect of diabetes on cognitive function. Both type 1 and type 2 diabetes mellitus have been associated with reduced performance on numerous domains of cognitive function. The exact pathophysiology of cognitive dysfunction in diabetes is not completely understood, but it is likely that hyperglycemia, vascular disease, hypoglycemia, and insulin resistance play significant roles. Modalities to study the effect of diabetes on the brain have evolved over the years, including neuro cognitive testing, evoked response potentials, and magnetic resonance imaging. Although much insightful research has examined cognitive dysfunction in patients with diabetes, more needs to be understood about the mechanisms and natural history of this complication in order to develop strategies for prevention and treatment.

In conclusion, there have been significant gains in understanding of the effect of diabetes on cognitive dysfunction. Evidence from neuro cognitive testing suggests that cognitive dysfunction should be listed as one of the many complications of diabetes, along with retinopathy, neuropathy, nephropathy, and cardiovascular disease. Cognitive function evaluation is a mandatory process in both prediabetic and diabetic condition and focused intervention specific to the dysfunction is essential in these diseases.

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