Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/0741t925

THE IMPACT OF DIABETES MELLITUS 2 IN DECLINE OF CEREBRAL FUNCTIONS

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Abstract:
Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycaemia, due to either a deficiency of insulin secretion or to a combination of insulin resistance and inadequate insulin secretion to compensate. The term diabetes was originally introduced to describe the clinical symptoms associated with unduly high glucose levels. Diagnostic emphasis then shifted to the glucose levels themselves and in addition to diabetes a milder level of hyperglycaemia denoted impair glucose tolerance has been defined by the W.H.O. It affects all the systems in the body. It affects functions of cerebrum in brain. Cerebrum is important and larger part of brain. It controls major functions of body. The present study is an attempt to study impact of Diabetes mellitus 2 in decline of cerebral functions.

Keywords: Diabetes, Cerebrum, Functions, hyperglycaemia

❖ Introduction:

The prevalence of Diabetes is 9.3 % in World.[1] 90% of this is comprised of type two diabetes mellitus. Diabetes is a disease known from the dawn of civilization. Sedentary life style, Lack of exercise, Faulty food habits and improper medication and Urbanization precipitate the disease Diabetes mellitus is a common chronic metabolic disorder prevalent all over the world. Although diabetes has been a known morbidity since time immemorial, its incidence has been growing notably in recent years. It has turned out to be the biggest “silent killer” today in the world. The mortality rate due to Diabetes mellitus is very high and is ranked fifth amongst the ten major causes of death in southern part of India. The Indian Council for Medical Research has focused attention on six diseases out of the several refractory diseases. These are Anal fistula,Viral hepatitis, Urolithiasis, Filariasis and Diabetes Mellitus.

The rising prevalence of diabetes is closely associated with industrialization and socio-economic development. It will soon become the first incommunicable disease whose severity will be endorsed by the United Nation. According to data released by the International Diabetes Federation, 41 million of the 659 million people in the age group of 20-79 years in India have diabetes. Currently the number of cases of Diabetes worldwide is estimated to be around 150 million. The prevalence

of Type II D.M. is expected to rise more rapidly in future because of increasing obesity and reduced physical activity. It has adverse effect on cerebral functions.

❖ **Aims** –
To study in detail The Impact of Diabetes Mellitus 2 on cerebral functions.

❖ **Objective:**
1. To take various references related to Diabetes Mellitus.
2. To take various references related to Cerebrum.
3. To understand the Impact of Diabetes Mellitus 2 on cerebral functions.

❖ **Material and Methods:**
Literature review is done through all available texts, various research papers available in Journals and online data available.

❖ **Review of Literature:**
➢ **Diabetes mellitus:**
▪ **Etymology:**
The word Diabetes is originated from the French word named "Jiyabatis" which means punctured pitcher or a pitcher with a leak, so that the water sprinkles out of it. The word diabetes is derived from the diobos a fountain meaning similarto that of the fountain.
Greek language the 'Diabetes' means 'to run through a siphon' and the term 'Mellitus' means honey.

▪ **Definition:**
Diabetes mellitus comprises a group of common metabolic disorder that share the phenotype of hyperglycemia. Factor contributing to hyperglycemia may include reduced insulin secretion decreased glucose usage, and increased glucose production.

▪ **Classification:**
Diabetes Mellitus in classified into -
1. Type 1 diabetes (usually leading to absolute insulin deficiency)
2. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretary defect with insulin resistance)

▪ **Insulin biosynthesis, secretion, and action**
Insulin is the hormone secreted by the beta cells of the islets of langerhans and derives its names from the Latin word INSULA which means an island. It was extracted from the pancreas by Banting and Best in 1921 and was isolated in crystalline form by Abel in 1930.

▪ **Synthesis and Storage**:
Insulin is synthesized within the beta cells which are situated in the tail of the pancreas. It is synthesized as a single chain polypeptide precursor called preproinsulin which is converted to proinsulin. Proinsulin is biologically $1/8^{th}$as active as insulin and forms only 3-6 % of the total insulin within the pancreas. It is not stored within the beta cells but is soon cleaved by protelytic enzymes after it has folded upon itself and the two disulfide bridges formed.

Thus is formed the single chain of C peptide and insulin, the A and B chains of which are connected by two disulfide bridges. Now insulin is packaged within granules and stored within beta cells from which is released at a slow rate, in repeated pulses, in to the circulation. Storage is facilitated by Zinc which makes insulin less soluble.

▪ **Pathogenesis of type 2 Diabetes Mellitus:**

While much has been learned in recent years, the pathogenesis of Type 2 diabetes remains enigmatic. There is no evidence that autoimmune mechanisms are involved. Life style clearly plays a role,as will become evident when obesity is considered. Nevertheless, genetic factors are even more important than in type 1 diabetes. Among identical twins, the concordance rate is 60% to 80%. In first-degree relatives with type 2 diabetes (and in non identical twins) the risk of developing disease is 20% to 40%, versus 5% to 7% in the population at large.

The two metabolic defects that characterize type 2 diabetes are:

(1) A derangement in ß-cell secretion of insulin and

(2) A decreased response of peripheral tissues to respond to insulin (insulin resistance).

The primacy of the secretary defect versus insulin resistance is a matter of continuing debate.

▪ **Deranged ß-Cell Secretion of Insulin**

In populations at risk for developing Type 2 diabetes (relatives of patients), a modest hyperinsulinemia may be observed, attributed to ß-cell hyper responsiveness to physiologic elevations in blood glucose. With the development of overt disease, the pattern of insulin secretion exhibits a subtle change. Early in the course of type 2 diabetes, insulin secretion appears to be normal and plasma insulin levels are not reduced. However, the normal pulsatile, oscillating pattern of insulin secretion is lost and the rapid first phase of insulin secretion triggered by glucose is obtunded. Collectively, these and other observations suggest derangements in ß-cell responses to hyperglycemia early in type 2 diabetes, rather than deficiencies in insulin

Later in the course of type 2 diabetes, a mild to moderate deficiency of insulin develops, which is less severe than that of type I. The cause of the insulin deficiency is not entirely clear, but-irreversible ß -cell damage does appear to be present. Unlike type 1 diabetes, there is no evidence of viral or immune-mediated injury to the islet cells. According to one view, all the somatic cells of predisposed individuals, including pancreatic ß cells, are genetically vulnerable to injury, leading to accelerated cell turnover and premature aging, and ultimately to a modest reduction in ß-cell mass. Chronic hyperglycaemia may exhaust the ability of ß cells to function (this is unfortunately called "Glucose toxicity"), as a consequence of persistent ß cell stimulation.

▪ **Insulin Resistance:**

Although insulin deficiency is present late in the course of type 2 diabetes, it is not of sufficient magnitude to explain the metabolic disturbances. Rather, reduced responsiveness of peripheral tissues (insulin resistance) is a major factor in the development of type 2 diabetes. At the outset, it should be noted that insulin resistance is a complex phenomenon that is not restricted to the diabetes syndrome. In obesity and pregnancy (gestational diabetes), insulin sensitivity of target tissues decreases (even in the absence of diabetes), and serum levels of insulin may be elevated to compensate for insulin resistance.

The molecular bases of insulin resistance are not clear. There may be a decrease in the number of insulin receptors, and more important, post receptor signalling by insulin is impaired. Binding of insulin to its receptors leads to translocation of GLUTs to the cell membrane, which in turn facilitates cellular uptake of glucose.

It is suspected that reduced synthesis and translocation of GLUTs in muscle and fat cells underlies the insulin resistance noted in obesity as well as in type 2 diabetes. Other post receptor signalling defects have also been described. From a physiologic standpoint, insulin resistance, regardless of its mechanism, results in

1. The inability of circulating insulin to properly direct the disposition of glucose (and other metabolic fuels),
2. A more persistent hyperglycaemia,
3. More prolonged stimulation of the pancreatic ß cell.

- **Clinical Features:**

- Polyuria and thirst
- Weakness or fatigue
- Ketoacidosis
- Recurrent blurred vision
- Vulvovaginitis /Pruritis
- Peripheral Neuropathy
- Often asymptomatic

- **Cerebrum:**[2]

The cerebrum is the large upper part of the brain. It is divided into cerebral hemispheres. In the human skull, the cerebrum sits atop the brainstem, with the cerebellum underneath the rear portion.

- **Function**

The cerebrum itself houses the four major lobes, and each lobe as its own set of functions. So although the cerebrum as a whole controls numerous functions in the body, this is mainly due to the function of each individual lobe and the interplay between them.

In general, the cerebrum controls all voluntary actions. It is also the control centre for:

- sensory processing
- emotional control
- motor control
- personality
- learning
- problem solving
- language and speech
- visual information
- spatial information
- cognition and higher thought
- imagination
- creativity
- music interpretation

Areas in the cerebrum are responsible for receiving and interpreting much of the physical world around the body. The sections below will detail which lobe controls which processes.

Frontal lobe

- speech
- behaviour and personality
- emotions
- body movement
- intelligence and self-awareness

Parietal lobe

- language and symbol use
- visual perception
- sense of touch, pressure, and pain
- giving meaning to signals from other sensory information

Temporal lobe

- memory
- hearing

- understanding language
- organization and patterns

Occipital lobe

- light
- colour
- movement
- spatial orientation

▪ **Impact of Diabetes Mellitus 2 on cerebral functions:**

- White matter pathology is also linked to cognitive loss and dementia observed in individuals with diabetes. Patients with type 2 diabetes have a higher risk of dementia than those with type 1 diabetes because of metabolic risk factors such as obesity, hypertension, and hyperlipidemia.[3,4]
- White matter illness is characterized by micro vascular abnormalities in the brain vessels, which show up as hyper intensities on MRI. It was discovered that patients with T2DM, HbA1C >7%, and pre-diabetes had greater white matter hyperintensities.[5]
- In addition, they result in brain atrophy, lacunar infarcts, and a reduction in white matter volume. Research with imagination has demonstrated that DM also modifies white matter tract function and connectivity. There has been evidence of a decline in white matter connectivity in both T2DM and Prediabetes. Poor performance in memory, attention, and executive functioning results from these changes.[6]
- Elevations in serum glucose have also been associated with increased beta-amyloid, which blocks neuronal transmission. Research has indicated that a diabetic's brain has higher levels of beta-amyloid and neurofibrillary tangles. This brain's capacity to consume and digest glucose is diminished.[7]
- Decreases in glucose processing have been linked to behavioural abnormalities, cognitive impairment, and trouble locating words.[8]
- The Alzheimer's Disease brain also had decreased glutamate levels and N acetyl aspartate, which results in gliosis and a loss of neuronal integrity.[9]
- Parietal and frontal lobe glucose metabolism was found to be reduced in Alzeimer's Disease patients according to PET scan results.[10]
- A persistently raised blood glucose level is associated with a very significant risk of cognitive impairment and microstructural changes in the white matter tracts. Cognitive dysfunction in individuals with type 2 diabetes is characterized by insufficient attention that affects work, executive function, mental processing, and memory recall.
- As people age, T2DM and dementia become more common.
- When cerebral ischemia occurs, elevated blood glucose levels aggravate neurologic damage, and even mild hyperglycemia increases the risk of further neurologic damage and delayed recovery.[11]

❖ **Discussion and Conclusion:**

We have therefore compiled the majority of the pertinent literature in order to better understand the different connections between hyperglycaemia and its effects on the cerebrum, which was the goal of this review. The clinical burden of diabetes and its complications is steadily rising, and risk factors such as obesity are becoming more and more prevalent worldwide. Decreases in cognitive performance and structural alterations in the brain are linked to diabetes mellitus. Neuropsychological testing has demonstrated mild to moderate decreases in cognitive performance in people with type 2 diabetes when compared to non-diabetic controls. A 50% higher incidence of dementia has also been linked to type 2 diabetes (T2DM).Diabetes mellitus (type 1 and type 2) is linked to mild to moderate declines in cognitive function. The underlying Pathophysiology of cognitive impairment varies significantly between type 1 and type 2 diabetes. Micro vascular problems and persistent hyperglycaemia are significant risk factors shared by type 2 diabetes.

T2DM is typically identified later in life and is frequently linked to insulin resistance, obesity, dyslipidemias, hypertension, and hypertension—all of which can have detrimental effects on the brain.

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