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DEMENTIA IN DIABETES: A REVIEW

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INTRODUCTION

The world health organization definition of diabetes is for a single raised glucose reading with symptoms, otherwise raised values on two occasions, of either[1]: Fasting plasma glucose >, 7.0 mmol/l (126 mg / dl) on with a glucose tolerance test, two hours after the oral dose a plasma glucose >> 11.1 mmol/l (200 mg / dl). A Glycated Hemoglobin of greater than 6.5% is another method of diagnosing diabetes[2] as is random blood sugar of greater than 11.1 mmol/l (200 mg / dl) in association with typical symptoms.[3] Globally as of 2010 it is estimated that there are 258 million people diabetes with type 2 making up about 90% of the cases. The term" Dementia '' refers to the clinical syndrome of impairment in multiple domains of cognitive function, which must include memory in a patient who remains alert with normal arousal.[4] A recent survey done by Harvard university School of public Health and the Alzheimer's Europe consortium revealed that the second leading health concern (after cancer) among adults is Dementia.[5] We will explore the complex relationship between Dementia and Diabetes in this review.

DIABETES AND DEMENTIA TYPES-RELATIONSHIP.

Compared to people without diabetes, people with diabetes have a greater rate of decline in cognitive function and a greater risk of cognitive decline.[6] Geert Jan Biessels et al, identified 14 eligible longitudinal population based studies if variable methodological quality to understand relationship between diabetes and major types of dementia's.The finding of mechanistic studies suggest that vascular disease and alternations in glucose, insulin, and amyloid metabolism underlie the pathophysiology but which of these mechanisms are clinically relevant in unclear.[7] Multiple interactions,some of which are yet to be elucidated

may underlie the relationship.

PATHOGENESIS.

Molecular defects associated with the development of diabetes also contribute to increased risk of all – types of dementia, including Alzheimer's disease, Vascular dementia and picks disease[8] Rita pilla et-al evaluated the association of diabetes alone combined with the Apoliprotien E (APOE) gene with incident Dementia and Neuropathological outcomes in a population based cohort of 2574 Japanese – American men enrolled in the Honolulu's – Asia Aging study including 216 subjects who underwent autopsy, type 2 diabetes was associated with total dementia, Alzheimer's disease and Vascular dementia. Individuals with both type 2 diabetes and the APOE E4 allele had RR of 5.5 for AD compared with those with neither risk factor. Participants with type 2 diabetes and E4 allied had a higher number of hippocampal neurotic plaques and neurofibrillary tangles in the cortex and hippo campus and they had a higher risk of cerebral amyloid angioplasty. The association between diabetes and AD is particularly strong among carriers of APOE E4 allele. The Neuropatho logical data are consistent with the clinical results.[9]

F. Pasquier et.al. also found evidence for an elevated risk of both Vascular Dementia, Alzheimer 's disease in Patient with Diabetes Mellitus type 2, albeit with strong interaction of other factors such as Hypertension, Dyslipedemia, APOE genotype diabetes is an independent predictor of post stroke dementia. Diabetes Mellitus being an atherogenic risk factor, it may increase risk of dementia through association with stroke, causing Vascular dementia and also stable perfusion abnormalities through glycosylated products may exacerbates Alzheimer's disease through direct interaction between the two pathological process or through cognitive impairment secondary to Cerebrovascular disease unmasking Alzheimer's disease at an earlier stage than it would otherwise be apparent. Increased risk of AD may also be mediated by the exacerbation of B- amyloid Neurotoxically by advance glycosylation end products identified in the matrix of Neurofibrillary tangles and amyloid plaques in AS brains or association with insulin function decreased cholinergic transport across blood brain barrier observed in diabetic animals may exacerbate cognitive impairment in AD.[10]

PATHOPHYSIOLOGY

Population based studies have shown that those with type 2 diabetes mellitus have an increased risk of cognitive impairment, dementia and Neurodegeneration. There are many

mechanisms through which diabetes could increased risk of dementia, including glycemia, insulin resistance, oxidative stress, advanced glycation end products, inflammatory cytokines and micro vascular disease[11] Krabbe et al found that low levels of BDNF accompany impaired glucose metabolism, decreased BDNF may be pathogenic factor involved not only in dementia and depression, but also in type 2 diabetes, potentially explaining clustering of there condition in Epidemiological studies.[12]

Chin cheng Hsu et al found that incidence of dementia is increased in diabetes mellitus type 2 and reduced by the use of sulfonylurea and metformin.[13] Studies by A.Ott et-al suggested that Alzheimer's disease may be more frequent in elderly diabetic patients treated with insulin.[14]

Welll Xu et-al concluded that borderline diabetes is associated with increased risk of dementia and Alzheimer's disease, the risk effect is independent of the future development of diabetes borderline diabetes may interact with severe systolic Hypertension to multiply the risk of Alzheimer's disease[15] W.L. Xu et al found that diabetes mellitus increased the risk of dementia and vascular dementia is especially very high when diabetes mellitus occur together with severe systolic hypertension or heart disease[16], Rachel A. whitemer et al found that among older patients with type 2 diabetes, a history of severe hypoglycemia episodes was associated with greater risk of dementia whether minor hypoglycemia episode increase risk of dementia is unknown[17] J.D. curb et al found no association between AD and diabetes, present either 25 or 15 years previously, was found after adjustment for age and education in a multiple regression model. A significant association was found between impaired glucose tolerance at baseline and Vascular dementia.[18]

DEMENTIA AND OTHER VASCULAR RISK FACTORS.

Kloppenburg et al conducted longitudinal population based studies that assessed the incidence of dementia in relation to Diabetes Mellitus, Hypertension, Dyslipedaemia or obesity was included. All 4 risk factors were associated with increased risk of dementia, but results of studies on diabetes and obesity were most consistent. At midlife, the population attributable risk of dementia was highest for Hypertension up to 3% of cases of late life dementia later in life diabetes appear to convey the highest risk of dementia[19] whitemer et al found that presence of multiple Cardio vascular risk factors at mid life substantially increased risk of later use dementia in a done dependent manner.[20]

CONCLUSION

These is substantial evidence that acute hypo and Hypoglycemia have disruptive effects on CNS, although relatively less is known about the slowly developing end - organ damage to CNS that may represent of cognitive by electrophysiological and structures changes and impairment of cognitive functioning.[21] Furthermore it has been shown that insulin affects several brain functioning including cognition and memory and reveals clinical studies have established links between insulin, resistance, Diabetes Mellitus and AD (Gasparine et.al 2002) recent evidence indicates that insulin regulates the metabolism of AB and tau proteins, which are involved in the formation of two humorless of Alzheimer's disease, AB deposits and Neurofibrullarly tangles, respectively (mandelkow et al 1992, Solano et al 2000, Gasaparise et al 2001).[21] Although AD and Diabetes Mellitus posses several overlapping fractures, mitochondrial dysfunction is one of the most relevant suggesting that mitochondria is a bridge between both disease.[21]

CHALLENGES AHEAD.

Though significant amount of work has been done to elucidate the relationship between Diabetes Mellitus and different types of dementia, Lot need to be done to understand complex associations which are directly or indirectly helpful in presenting cognitive decline in diabetic patients.

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