Study Of Dementia With Particular Reference To Mini Mental State Examination And Geriatric Depression Scale In Diabetic Patients

Abdul Rahiman Rahmath[1], Pattath Sadanandhan Krishnaprabha[2], Varma Sana[3], Pichakacheri Suresh Kumar[4], Edakkot Sreekumaran[5*]

[1]Research Scholar, Department of Life Sciences, University of Calicut., Malappuram.
[2]Lecturer in Physiology, PNNM Ayurveda College, Cheruthuruthy, shoranur.
[3]Lecturer in Physiology, Bethany Navajeevan College of Physiotherapy, Trivandrum.
[4]Physician and Diabetologist, Diabcare India, Vandipetta, Calicut.
[5]Reader in Physiology, Department of Life Sciences, University of Calicut, Malappuram.

Abstract

To detect the effect of dementia related problems on a person's cognitive functions, especially memory and the occurrence of depression like symptoms by using Mini Mental State Examination (MMSE) and Geriatric Depression Scale (GDS). The subjects were divided into three, one as general group who are non- diabetic, second as control group who are diabetic and non- neuropathic and the third as test group, who are diabetic as well as neuropathic. The six parameters analyzed were age, gender, duration of diabetes, family history of diabetes, Body Mass Index (BMI) and food habits. The scores were then statistically analyzed using SPSS (Statistical Package for Social Sciences, 12.0.1). The results in the present study reveal that there is a decline in the cognitive performance in MMSE based on gender, but in the case of age and duration of diabetes, the test group subjects showed a poorer performance. A decline in MMSE score shows greater risk for cognitive impairment. Similarly GDS scores also support this result.Diabetic neuropathic patients poorly performed in MMSE and GDS when compared to non- neuropathic patients. Diabetes has a significant role in the deterioration of cognitive function. Females showed poor performance than males. As age and duration of diabetes progresses, the chance for memory loss and depression increases. Food habits have no significant role as per this study.

Key Words: Cognition, Diabetes, GDS, MMSE, Neuropathy.

INTRODUCTION

Diabetes is a group of metabolic disorder charactrerized by hyperglycemia resulting from decrease in secretion of insulin (Type 1DM /IDDM) and also be due to insulin resistance (Type 2DM /NIDDM)[1] . Insulin is the hormone that allows glucose to be released into the blood and taken up by the cells ,where it is utilized for energy . Diabetes is one of the "diseases of civilization" ,with interaction of genetic ,nutritional and socio - cultural factors among others , whose results prevail as the highest pathologies in Western countries.

Diabetes is a risk for atherosclerosis and is an additive factor for large vessel diseases ,e g . smoking ,hypertension and hyperlipidaemia[2] . These complications are called macro vascular diseases .Whereas in the case of micro vascular disease , small vessels are affected throughout the body ,but the disease process is potentially a danger in 3 sites :the retina ,the renal glomerulus and the nerve sheath.

Diabetic neuropathy is a consequence of micro angiopathy, which is thought to result in micro vascular infarcts with loss of nerve fibers within the nerve trunks. However, its pathogenesis also seems to be associated with certain metabolic alterations. Typically neuropathy is evidenced by a slower nerve conduction rate[3].

Clinical findings include symmetric impairment of distal proprioception, loss of tactile and vibratory sensations as well as loss of osteotendinous reflexes. These alterations are usually associated with dysesthesia and hyperesthesia. Sensory loss in the foot predisposes to the development of chronic ulcers and Charcot's joints. The appreciation of touch, pain and temperature sensation is lost and proprioception in the lower limb is absent as that seen in peripheral neuropathy. In diabetic patients with severe neuropathy the impairment of sensory pathway is examined[4]. These studies are co-related with cognitive studies to detect whether the same sort of impairment is caused in the upper motor neuron level also. Testing the cognitive function assesses the impairment of the upper motor neuron function.

Dementia and diabetes mellitus are two of the most prevalent problems in older people[5] .More than 10 % over the age of 65 years develop dementia and the prevalence of dementia increases to more than 50 % of people over age 85 . More than 10 % of the elderly suffer from diabetes ,and the prevalence is increasing . Type 2 diabetes is a common disease in old age affecting about 20 %over the age of 65 years[6] . Studies have been reported that dementia is related to diabetes and lower levels of cognitive function[7] .

Address for correspondence*
Dr. E.Sreekumaran,
Reader in Physiology, Department of Life Sciences, Calicut University. Malappuram, Kerala, India. 673635.
Email: drsreekumaran@gmail.com Ph. No- +91- 9539254721
Fax: 0494 -2400269

METHODS

The test was conducted on a total of 150 subjects (64 males and 87 females of the age of 50 +20yrs). Among the 150 volunteers 48 of them were considered as test group and the other 52 as control group . The general group consisted of 50 volunteers .The test group consisted of diabetic patients with neuropathy and control group included diabetic patients without neuropathy and the general group were non diabetic and non neuropathic .The subjects for the study were from both in patients and out patients of P V S Hospital Calicut and from outpatients of Diabcare clinic ,Manjeri ,Malappuram . The study was followed after attaining the clearance of institutional ethical committee . To detect the risk of peripheral neuropathy in diabetic patients the following instruments were used .

Monofilament

It is used to detect large fibre neuropathy ,which is based mainly upon the sense of touch . The monofilament is a nylon filament (Purchased from Dhansai Laboratory Gurgaon Mumbai , India) which delivers a force of 10 grams when applied to the skin at the point of buckling .The filament is used at different regions of the sole ,the big toe ,first metatarsal ,third metatarsal ,fifth metatarsal , instep and heel respectively .The inability to feel this pressure indicates large fibre neuropathy.

Biothesiometer

Biothesiometer is a digital hand held vibration perception threshold analyzer with stabilized vibration generator (Purchased from Diabetik Foot Care India Pvt Ltd, Chennai, Tamil Nadu, India). It is an accurate tool to diagnose peripheral neuropathy. Loss of sensation due to neuropathy is the major cause of painless injuries to the feet. Early and accurate detection of sensation loss is the best way to protect foot from future amputation. It has been divided into two units; Vibration unit & thermal unit.

Materials For Cognitive Study

Mini Mental State Examination

Test Material

MMSE Questionnaire

It is a modified questionnaire by Folstein et al.,[8]. This modified version is developed by Indo-US Cross National Dementia Epidemiology Study and is a collaborative programme of University of Pittsburgh, School of Medicine, Dept. of Psychiatry, Graduate School of Public Health, US and Center for Aging Research in India, New Delhi, India.

PROCEDURE

Volunteers were made aware of the test and a written consent letter was obtained from them as per the guidelines of institutional ethical committee. MMSE include simple questions and problems covering several areas of cognitive functioning such as orientation to time and place, memory, attention and concentration, recognition of objects, language function, motor functioning and praxis. After completing the test, correct responses were given 1 point each and 0 for incorrect responses. The maximum score given is 30. Any score over 20 is effectively a normal value.

Geriatric depression scale

Test material

GDS questionnaire

It is a brief questionnaire coined by the Hartford Institute of Geriatric Nursing, in which the volunteers were asked to respond to 30 questions with 'YES' or 'NO'[9]. The volunteers were made aware of the test and a written consent letter was obtained from them as per the guidelines of institutional ethical committee. After collecting the personal details, experimenter asks the questions in numerical order. The volunteer was instructed to say 'Yes or No'. Responses is noted and scored. The scoring exhibited a positive relation with depression scores of 0-9 are considered as normal 10-19 mild depression and 20-30 indicated severe depression.

RESULTS

Significant at 5 % level, when the male population of test group was compared with female population of the same group In the gender based comparison of MMSE, the diabetic males with neuropathy gave a better performance when compared to their female counterpart. The mean values showed a statistical significance at 5 % level (Figure 1).

Significant at 5 % level, when control group was compared with the test group. In the age based comparison of GDS, the older diabetic group (>60) gave a poorer performance in comparison with the non diabetic and the diabetic- neuropathic lot of the same

Table 1: Comparison of performance of MMSE of General, Control and Test based on gender

Data	Male			Female		
	Mean	Standard Error	N	Mean	Standard Error	N
Non-diabetic (General)	28.59	0.5	17	28.91	0.272	34
Diabetic and non-neuropathic (Control)	27.62	0.480	21	26.32	0.571	31
Diabetic and neuropathic (Test)	26.42	0.555	26	23.36	1.008	22
Significance	0.043 (Between male and female in test group)					

Table 2: Comparison of Performance of GDS of General, Control and Test in the age groups above and below 60 years.

Data	<60			>60		
	Mean	Standard Error	N	Mean	Standard Error	N
Non-diabetic (General)	7.86	0.643	44	14.29	1.063	7
Diabetic and non-neuropathic (Control)	9.45	0.871	38	9.36	1.345	14
Diabetic and neuropathic (Test)	9.58	1.162	24	13.13	1.157	24
Significance	0.015 (Between General and Control)					
Significance	0.036 (Between control and Test)					

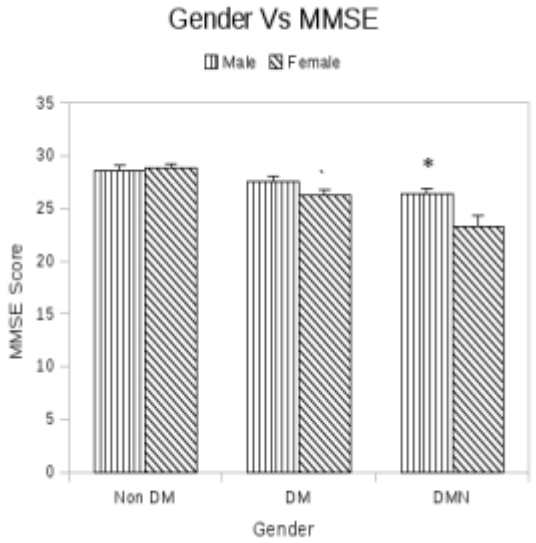

Figure 1:- Graph showing the comparison of MMSE based on gender [General (N=51), Control (N=52) & Test (N=48)].
Non DM: Non Diabetes Mellitus, DM: Diabetes Mellitus without neuropathy, DMN: Diabetes Mellitus with neuropathy.

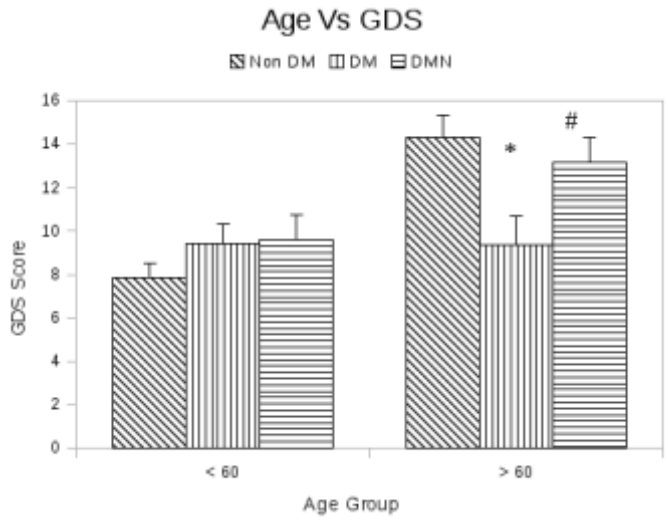

Figure 2:- Graph showing the comparison of GDS with age groups above and below 60 years [General (N=51), Control (N=52) & Test (N=48)].
Non DM: Non Diabetes Mellitus, DM: Diabetes Mellitus without neuropathy, DMN: Diabetes Mellitus with neuropathy.

Table3: Comparison of Performance of GDS of General, Control and Test based on gender.

Data	Male			Female		
	Mean	Standard Error	N	Mean	Standard Error	N
Non-diabetic (General)	7.29	1.111	17	9.47	0.784	34
Diabetic and non-neuropathic (Control)	7.00	0.819	21	11.06	0.916	31
Diabetic and neuropathic (Test)	9.92	1.285	26	13.05	0.981	22
Significance	0.035 (Between male and female in control group)					
		0.05 (Between male and female in test group)				

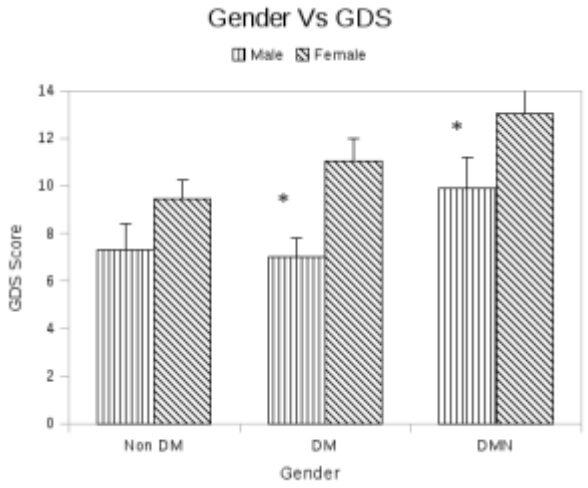

Figure 3: - Graph showing the comparison of GDS based on gender [General (N=51), Control (N=52) & Test (N=48)].
Non DM: Non Diabetes Mellitus, DM: Diabetes Mellitus without neuropathy, DMN: Diabetes Mellitus with neuropathy.

age group. The difference of their means was statistically significant at 5 % level (Figure 2).

Significant at 5 % level, when the male population of control group and test group was compared with the female population of control and test group. In the gender based comparison of GDS, the test and the control group female showed a poorer performance than males, also explains that neuropathy does not play a vital role in depression. The difference of their means was statistically significant at 5 % level (Figure 3).

DISCUSSION

Cognitive dysfunction is an important symptom of dementia. The etiology of dementia is complex and some cross-sectional studies suggest that diabetes may lead to cognitive decline caused by hypoglycemia, hyperglycemia, hyperinsulinemia and vasculopathy[10,11,12,13]. The results from the few prospective studies examining diabetes and change in cognitive function or incidence of dementia have been inconsistent. Here, in this study, cognitive impairment is assessed using the following tests; MMSE and GDS.

Performance of several MMSE items (immediate and delayed memory recall), completion of 3-step command and copying of figure should not depend on educational experience or current reading comprehension. But people with lower literacy were less able to perform serial subtractions. The ability to repeat "Neither this, nor that" depended on familiarity with this non-grammatical phrase and familiarity will depend on educational experience and culture[14]. Low MMSE score is directly related to the incidence of dementia[15].

Cognitive decline was significantly associated with socio demographic variable including age, education, marital status and house hold composition. In addition, respondents with repeated vision impairment, stroke and diabetes were at increased risk for cognitive decline[16].

In this study, the subjects were divided into general, control and test group based on diabetes, micro vascular complications and peripheral neuropathy. Control group performed better than the test group, and this shows that diabetic neuropathy causes decline in cognitive functioning than in non-neuropathic patients. Stroke and peripheral neuropathy are recognized neurological complications of diabetes and epidemiological evidence is now emerging to implicate the prediabetic state of impaired glucose tolerance as a risk factor for these conditions[17] and also consider the possibility of a link between impaired glucose tolerance and cognitive dysfunction.

When compared to the general population (i.e., non diabetic), diabetics showed increased risk of cognitive impairment. Cognitive ability was indexed by means of MMSE. The result showed that diabetics perform significantly worse on the MMSE than do the non-diabetics and the result was found to be similar to the study conducted by Nilson et al.,[18].

Subjects were again categorized based on their age into two groups and this comparison is statistically analyzed in various combinations. In the comparison of general, control and test group of the age group <60 and >60, there is no significant difference in MMSE. This suggests that there is no decline in cognitive functioning as age increases. But the studies reveal that age and education are more salient predictors of cognitive deterioration. Other socio-demographic and several medical conditions including stroke and diabetes should be considered a part of cognitive aging studies among Mexican American elders, [16,19, 20, 21,22.]

In this study, based on gender, different combinations were analyzed. Significant difference was found between males and females of the test group. From figure: 1 we can assume that the females performed poorer than the males. Some studies but not all have shown that gender is a variable that could influence cognitive performance[12, 23]. Estrogen, which markedly decreased after menopause, deteriorate particularly associated with hippocampal functions such as memory, cognition and autonomic control[24].

In the comparison based on the duration of diabetes, test and control groups are found to be not significantly different. The association between diabetes and cognitive function was bit more pronounced in whom diabetes was diagnosed for 12 or more years[25]. Duration of diabetes was related to diminished cognition in a dose response manner that was independent of age and co morbid conditions such that women with diabetes for 15 years or longer held up to a threefold increased risk of baseline cognitive impairment and more than a double risk for major cognitive decline. The risk of both cognitive impairment and decline was greatest for women with diabetes with duration of at least 15 years[26].

Depression and cognitive impairment are among the most important mental health problems in elderly people. Both conditions have severe consequences, including diminished quality of life, functional decline and high mortality. Late onset depression and cognitive impairment often occur together, suggesting a close association between them. It is not known, however, whether depression leads to cognitive decline or vice versa. Clinical practice and research evidence suggests that depression precedes cognitive decline in old age[27,28].

Siddiqui et al., [29] determined the prevalence of depression and its relation with concomitant disorders and social status among the diabetics. Depressed patients suffered from a wide range of other diseases like Alzheimer's disease, vascular dementia, hypertension, diabetes mellitus, osteoporosis,

bronchial asthma and osteoarthritis[30,31,32,33].

Depression is the most common of the reversible causes of memory impairment, and people with diabetes are twice as likely to suffer from depression as those without diabetes. Recent evidence suggests that diabetes may create alterations in the regions of the brain that are associated with cognition and increase the risk for developing a depressive disorder[34]. Fortunately, problematic medications can be modified and alcohol misuse or depression can be treated. Unfortunately, despite its relevance to the course of diabetes, depression is recognized and treated in less than one-third of people with diabetes[35].

In the comparison of general, control and test groups, GDS scores have no significant difference with respect to family history of diabetes. So, family history is not a significant factor for GDS. From the result we can assume that it is not the family history but the severity of the disease, which accounts for the condition.

In the case of food habit (vegetarian/non vegetarian) the comparison of general, control and test is found to be not significant and this may be due to the less number of vegetarian subjects involved in this study. A low frequency of fish consumption was significantly reported to be associated with depression in women, but not in men[36].

In the case of age groups the comparison of the general, control and the test groups (Figure: 2) showed significant difference. In the age group of >60, the control group performed better than the test group. From this result we assume that age is an important factor in the case of depression. Studies reveal that depression is seen at high rate in older people[37,38].

The comparison based on gender was also found to be significant in GDS. As shown in figure: 3, females showed greater risk of depression than males. It may be due to the influence of hormones that may be contributing to the increasing rate of depression in women particularly during menstrual cycle changes, pre-menopause. Estrogen therapy in postmenopausal women is reported to slow the decline in cognitive function[39]. In males, increased memory is due to the action of testosterone. Short-term testosterone administration enhances cognitive function in healthy older men. However, it remains unclear whether these improvements in cognition are attributable to increased testosterone or estradiol levels or both. The potential role of testosterone Vs its metabolites on cognition requires further research[40].

The strongest predictors of this liability were, in descending order, 1) stressful life events, 2) genetic factors, 3) previous history of major depression and 4) neuroticism[41]. Many women face additional stress such as responsibilities both at work and home, single parenthood and caring for children and aging parents. Men are less likely to suffer from such depressions[42].

CONCLUSION

A poor performance in MMSE score shows greater risk for cognitive impairment. Similarly GDS scores also support this result. Diabeteic neuropathy has a significant role in the deterioration of cognitive function because diabetic neuropathics poorly performed in MMSE and GDS when compared to non-neuropathics. The chance for memory loss and depression increases as age and duration of diabetes progresses. In the case of Gender, males performed better than females both in MMSE and GDS. Food habits have no significant role in this study.

REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes. Diabetes care. 2006;29(1):43-48.
2. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, Other Risk Factors, and 12-Yr Cardiovascular Mortality for Men Screened in the Multiple Risk Factor Intervention Trial. Diabetes care. 1993; 16(2): 434-444.
3. Callaghan BC, Stables CL, Smith AL, Feldman EL. Diabetic neuropathy: clinical manifestations and current treatments. The lancet. 2012; 11(6):521-534.
4. Maser R, Nielsen V, Bass EB, Manjoo Q, Dorman JS, Kelsey SF. Measuring Diabetic Neuropathy: Assessment and Comparison of Clinical Examination and Quantitative Sensory Testing. Diabetes care. 1989; 12(4):270-275.
5. Abendelhafiz AH, Sinclair AJ. Management of type 2 diabetes in older people. Diabetes Therapy. 2013;4(1):13-26.
6. Arvanitakis Z, Wilson RS, Bienias JL, Evans DA, Bennett DA. Diabetes Mellitus and Risk of Alzheimer Disease and Decline in Cognitive Function. Journal of Archives of Neurology. 2004; 61(5):661-666.
7. Cukierman T, Gerstein HC, Williamson JD. Cognitive decline and dementia in diabetes—systematic overview of prospective observational studies. Diabetologia. 2005; 48(12):2460-2469.
8. Folstein MF, Folstein SE and McHugh PR. Mini Mental State- A practical method for Grading the Cognitive State of Patients for the Clinician. Journal of Psychiatric Research. 1975; 12(3):189-198.
9. Yeasavage JA, Brink TL, Lum O, Hunge V, Adey M and Leirer VO. Development and validation of Geriatric screening scale. Journal of Psychiatric Research. 1983; 17(1):37-49.
10. Stewart R, Liolitsa D. Type 2 diabetes mellitus, cognitive impairment and dementia. Journal of Diabetic medicine. 1999;16(2):93-112.
11. Reaven G, Thompson LW, Nahum D, Haskins E. Relationship Between Hyperglycemia and Cognitive Function in Older NIDDM Patients. Diabetes care. 1990; 13(1):116-121.
12. Gregg EW, Yaffe K, Cauley JA, Rolka DB, Blackwell TL, Narayan VKM, Cummings SR. Is Diabetes Associated With Cognitive Impairment and Cognitive Decline among Older women?. Archives of internal Medicine. 2000; 160(2):174-180.
13. Ghasemi R, Dargahi L, Haeri A, Moosavi M, Mohamed Z, Ahamadiani A. Brain Insulin Dysregulation: Implication for Neurological and Neuropsychiatric Disorders. Molecular Neurobiology. 2013; 47(3): 1045-1065.
14. Baker DW, Gazmararian JA, Sudano J, Patterson M, Parker RM and Williams MV. Health Literacy and performance on Mini Mental State Examination. Aging and Mental Health. 2002; 6(1): 22-29.
15. Croxson SC and Jagger C. Diabetes and cognitive

impairment – a community based study of elderly subjects. Age and Aging. 1995; 24(5): 421-424.

16. Nguyen HT, Black SA, Ray LA, Espino DV and Markides KS. Predictors of decline in MMSE Scores among Older Mexican Americans.The Journals of Gerontology. 2002; 57(3):181 – 185.
17. Robinson SJ and Smith AG. Therapy insight: Neurological complication of pre- diabetes. Nature clinical practice neurology. 2006; 2: 276-282.
18. Nilson E, Fastborn J, Wahlin A. Cognitive Functioning in a population Based Study of old Non- demented Non-depressed persons: The Impact of Diabetes. Archives of Gerontology and Geriatrics. 2002; 35(2): 95-105.
19. Anstey KJ, Sanden CV, Salim A and O'Kearney R. The smoking as a risk factor for dementia and cognitive decline: A Meta Analysis of prospective studies. American Journal of Epidemiology. 2007; 166(4): 367-378.
20. Fiona AM, Kari K, Fiona EM, Eugene P, Peter BJ, Michaele D and Carol B. Prevalence of depression in older people in England and Wales: The MRC CFA study. Psychological medicine. 2007; 37: 1787-1795.
21. Raiha I, Raimo I, Ojanlatva A, Viramo P, Sulkava R and Kivela S. Poor performance in Mini Mental State Examination due to causes other than dementia. Scanadian Journal of Primary Health care. 2001; 19(1): 34-38.
22. Brands AMA, Biessels GJ, Edward HF, De Hann DL, Kappelle J and Kissels RP. The Effects of Type I Diabetes on Cognitive Performance. Diabetes Care. 2005; 28(3): 726 – 735.
23. Gao S, Hendrie HC, Hall KS and Hui S. The relationships between age, sex and the incidence of dementia and Alzheimer's disease; A Meta Analysis. Archives of General Psychiatry. 1998; 55(9): 809-815.
24. Genazzani AR, Bernardi F, Pluchino N, Begliuomini S, Lenzi E, Casarosa E and Louisi M. Endocrinology of menopausal transition and its brain implications. CNS Spectrum. 2005; 16:449-457.
25. Debling D, Amelang M, Hasselbach P, Sturmel T. Diabetes and Cognitive function in a population based study of elderly woman and men. Journal of diabetes and complications. 2006; 20 (4):238-245.
26. Hippel WV, Vasey MW, Gonda T and Stern T. Executive function deficit rumination and late onset depressive symptoms in older adults. Cognitive Therapy and Research. 2008; 32(4): 474-487.
27. Zubenko GS, Zubenko WN, Mc pherson S, Spoor E, Marin DB, Farlow MR, et al. A collaborative study of the emergence and clinical features of the major depressive syndrome of Alzheimer's disease. American Journal of Psychiatry. 2003; 160(5): 857-866.
28. Siddiqui MS, Fernandez HH, Garvan CW, Darrow LK, Bowers D, Rodriguez RL, et al. Inappropriate crying and laughing in Parkinson's disease and movement disorders. Journal of Biological Psychiatry. 2009; 10(3): 234-240.
29. Ertan FS, Ertan T, Kziltan G and Uygucgil H. Reliability and validity of the geriatric depression scale in depression in Parkinson's disease. Journal of Neurology, Neurosurgery and Psychiatry. 2005; 76(10): 1445-1447.
30. Andreia ZS, Monica ZS, Joao BS and Francisco LN Hypertension and depression. Clinics (2005) 60(3).
31. Sultzer DL, Levin HS, Mahler ME, High WM and Cummings JL. A comparison of Psychiatric symptoms in vascular dementia and Alzheimer's disease. American Journal of Psychiatry. 1993; 150(12):1806-1812.
32. Park JH, Lee SB, Lee TJ, Lee DY, Jhoo JH, Youn JC, et al. Depression in vascular dementia is quantitatively and qualitatively different from depression in Alzheimer's disease. Dementia and Geriatric Cognitive Disorders. 2007;23(2): 67-73.
33. Zrebiec J. Clinical Decision Making: Case Study: Cognitive Impairment, Depression, and Severe Hypoglycemia. Diabetes Spectrum. 2006; 19: 212-215.
34. Timonen M, Horrobin D, Jokelainen J, Laitinen J, Herva A and Rasanan P. Fish consumption and depression: the Northern Finland 1966 birth cohort study. Journal of Affective Disorders. 2004; 82(3): 447-452.
35. Kuo HK, Lipsitz LA. Diabetes may create alterations in the regions of the brain that are- Cerebral White Matter Changes and Geriatric Syndromes: Is There a Link?. The Journal of Gerontology series A. 2004; 59(8): 818-826.
36. Kyrozis A, Psaltopoulou T, Stathopoulo P, Trichopoulos D, Vassilopoulos D, Trichopoulo A . Dietary lipids and geriatric depression scale score among elders: The EPIC – Greece cohort. Journal of Psychiatric Research. 2009; 43: 763-769.
37. Philips ML, Drevets WC, Rauch SL and Lane R. Neurobiology of emotion perception 1: The neural basis of normal emotion perception. Biological Psychiatry. 2003; 54:515-528.
38. Hendrie HC. Epidemiology of dementia and Alzheimer's disease. American Journal of Geriatric Psychiatry. 1998; 6(2):S3-18.
39. Rosen HJ , Allison SC, Schauer GF, Tempini MLG, Howard J, Weiner MW and bruce LM. Neuro anatomical Correlatives of Behavioral Disorders in Dementia. Brain. 2005; 128(11): 2612-2625.
40. Warren MF, Serby MJ and Roane DM. The effects of testosterone on cognition in elderly men- A review. CNS Spectrums. 2008; 13(10):887 – 897.
41. Kendler KS, Kesler RC, Walter EE, Maclean C, Neale MC, Heath AC and Eaves AJ Stressful life events, genetic liability and onset of an episode of major depression in women. American Journal of Psychiatry. 1995; 152(6):833- 842.
42. Llaneza P, Garcae-Portilla MP, Suairez DL, Armott B,