PROFILE OF NEUROLOGICAL PROBLEMS IN DIABETES MELLITUS: RETROSPECTIVE ANALYSIS OF DATA FROM 1294 PATIENTS

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Data from 1294 patients with diabetes mellitus admitted to the Endocrinology Department of the Institute of Medical Sciences, Srinagar, Kashmir, from 1986 to 1994, were analyzed for frequency of various neurological problems. Of 1294 patients, 46.29% had clinical evidence of one or more neurological problems. The frequency of neurological problems was significantly more in patients with type II diabetes mellitus ($P<0.001$). Predominant neurological problems included peripheral neuropathy (96.66%), stroke (5.51%), Parkinsonism (1.50%), seizure disorder (1.17%) and dementia (1%). Mean (±SD) age of patients with neurological problems was significantly more ($P<0.001$) than those without neurological problems (52.07±9.52 versus 47.45±12.87 years for type II diabetes mellitus; 26.73±8.40 versus 18.0±3.62 for type I diabetes mellitus). Mean duration of diabetes in patients with neurological problems was significantly more than those without neurological problems (6.70±6.04 versus 3.95±4.22 years for type II diabetes mellitus; 5.63±3.67 versus 1.89±2.57 for type I diabetes mellitus). At the time of admission, fasting blood glucose was lower in patients without neurological problems as compared to patients with problems (9.08±2.22 versus 11.05±4.91 mmol/L for type II diabetes mellitus; 9.44±2.80 versus 13.01±5.01 mmol/L for type I diabetes mellitus; $P<0.001$). *Ann Saudi Med 1997;17(1):20-25.*

Diabetes mellitus (DM) constitutes a growing concern to the population of the world, predominantly because of the devastating effects of its chronic complications. So common and so definite are the chances of developing certain complications during the course of this "lifelong" disease that some of them have been regarded as "consequences" rather than complications.[1] Major long-term complications of diabetes are neuropathy, retinopathy, nephropathy and angiopathy. Peripheral neuropathy (PNP) is the most common chronic complication of diabetes mellitus and can involve almost any peripheral nerve. It is a major cause of morbidity among these patients.[1,2] Estimates of prevalence of diabetic PNP vary widely, between 10% to 100%.[2-6] Compared to complications in the peripheral nervous system, long-term diabetic complications in the central nervous system are relatively subtle and occur more frequently than is believed. Diabetes literature is replete with information on the vascular complications of neuropathy, nephropathy, retinopathy, coronary artery disease and peripheral vascular disease, but little information is available on the cerebrovascular disease in diabetic patients. This is surprising because diabetic patients have a two- to sixfold increased risk of thromboembolic strokes than the nondiabetic population, and stroke-related mortality and morbidity are increasing in the diabetic population.[6-10]

In this study, we retrospectively analyzed the data from 1294 patients with DM, for various neurological problems (NP), with particular reference to PNP and strokes. This study was conducted with the particular purpose of finding the pattern of NP in the diabetic population in a developing part of the world, where health care systems are nowhere near optimal.

Subjects and Methods

The medical records of 1294 patients with DM admitted to the endocrine division of the Institute of Medical Science (IMS), Srinagar, Kashmir (India), were screened for NP. Out of these, 167 patients had type I DM, 1087 patients had type II DM, and 40 were documented to have fibrocalculous pancreatic diabetes (FCPD). Patients with gestational diabetes, secondary causes of hyperglycemia (i.e., Cushing's syndrome, acromegaly, drugs, etc.) and those whose records were inadequate or diagnosis was not satisfactorily made, were excluded from

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Accepted for publication 18 June 1996. Received 6 May 1996.

TABLE 1. *Frequency of neurological problems (NP) in patients with different types of diabetes mellitus.*

Type of diabetes	# (%) of diabetics with NP	# (%) of diabetics without NP
Type I (n=167)	41 (24.55)	126 (75.45)
Type II (n=1087)	545 (50.14)	542 (49.86)
FCPD (n=40)	13 (32.5)	27 (67.5)
Total (n=1294)	599 (46.29)	695 (53.71)

X^2df_2=41.24, *P*<0.001 (significant).

TABLE 2. *Characteristics of diabetic patients with neurological problems.*

Characteristic	Type I DM (n=41)	Type II DM (n=545)	Statistical significance
Age (yr)			
Mean±SD	26.73±8.40	52.07±9.57	*P*<0.001 (S)
Range	11-45	26-75	
Sex			
Male:female	22:19	286:259	*P*>0.5 (NS)
Duration of diabetes (yr)			
Mean±SD	5.63±3.67	6.70±6.04	*P*>0.05 (NS)
Range	0.08-11	0.02-25	

S=significant; NS=nonsignificant.

TABLE 3. *Comparison between characteristics of type I diabetes mellitus patients with neurological problems (NP) and those without neurological problems.*

Characteristic	Patients with NP (n=41)	Patients without NP (n=126)	Statistical significance
Age (yr)			
Mean±SD	26.73±8.40	18.0±3.62	*P*<0.001 (S)
Range	11-45	2-40	
Sex			
Male:female	22:19	101:25	*P*<0.001 (S)
Duration of diabetes (yr)			
Mean±SD	5.63±3.67	1.89±2.57	*P*<0.001 (S)
Range	0.08-11.0	0.02-6.0	
Fasting blood-glucose*			
Mean±SD (mmol/L)	13.01±5.01	9.44±2.80	*P*<0.001 (S)

*Pretreatment in the hospital.

the study. The definitions and terms used during the analysis of the patient records are as follows: 1) Admission: only those patients specifically admitted for a diabetes-related problem. 2) Diabetes mellitus: all study subjects had DM established by WHO criteria and classified as type I or type II as defined by WHO.[11] 3) FCPD was diagnosed in patients with DM who had roentgenographic evidence of pancreatic calcification.[12] 4) Obesity: body mass index (BMI) of >27.8 in males and 27.3 in females. 5) Hypertension: previous treatment for hypertension, or blood pressure in the hospital >160/95 mmHg on two or more occasions in patients older than 40 years, or >140/90 mmHg in those 40 years or younger.[4] 6) Neuropathy: the minimum criteria was failure to elicit the knee and/or ankle reflexes after reinforcement with or without symptoms of neuropathy or gross sensory disturbance in both feet, in the absence of any other cause of neuropathy.[4,13] 7) Nephropathy: quantitative 24-hour urine protein excretion >500 mg per 24 hours in the absence of other renal disease.[4] 8) Renal insufficiency: serum creatinine >200 μmol/L (normal range 50-150 μmol/L.[4] 9) Retinopathy: fundi examined by ophthalmoscope by an ophthalmologist/endocrinologist and classified as background or proliferative retinopathy according to Kohner et al. classification.[14] 10) Coronary artery disease: clinical, electrocardiographic, echocardiographic or biochemical evidence of myocardial ischemia presenting as angina, myocardial infarction or congestive heart failure.[4] 11) Stroke: sudden or rapid onset of focal or global brain dysfunction of vascular origin, lasting for more than 24 hours in the absence of causes such as meningitis, space-occupying lesions (tumors, abscesses, etc.), traumatic cerebral hemorrhage and subdural collections, including hematoma. Stroke was considered to be thromboembolic when a focal neurological event occurred without prolonged unconsciousness, nuchal rigidity, fever, prominent leukocytosis or bloody spinal fluid. The diagnosis of hemorrhagic stroke was made when the neurological event was accompanied by headache, loss of consciousness and bloody spinal fluid and/or CT scan evidence of cerebrovascular accident, either transient or established.[4,8,10,15] 12) Parkinsonism: criteria for diagnosis were one or more of the following: diagnosis of parkinsonism made by a qualified neurologist; demonstration of all the three major manifestations of parkinsonism, resting tremor, bradykinesia and rigidity; and demonstration of exaggerated glabellar reflex, reduced facial expression and unilateral or significantly asymmetrical bradykinesia or rigidity. Among patients fulfilling these criteria, the etiologic subgroups were defined as follows: drug-induced parkinsonism was defined as a syndrome following the use of neuroleptics or other antidopaminergic agents in the six months preceding onset of symptoms and a negative history of symptoms preceding drug use. Parkinsonism in vascular disease was defined by the presence of at least two of the following findings: hypertension, emotional incontinence and pseudobulbar palsy, broad-based gait, definite history of stroke in the course of the illness, widespread pyramidal signs and abrupt onset with stepwise progression of symptoms. Parkinson's disease or idiopathic parkinsonism was defined by exclusion of all other possible causes of parkinsonism.[16,17] 13) Seizures: episodes of stereotyped disturbance of cerebral function presenting with impaired consciousness, convulsions, other motor, sensory,

somatosensory, autonomic or psychic features, associated automatic behavior which was not due to an acute cerebral insult, such as head trauma, infections of the central nervous system, stroke or acute or chronic metabolic disturbances such as hypoglycemia, metabolic acidosis, azotemia and other endocrinopathies.[15] 14) Dementia: progressive deterioration in the mental function of the individual in the presence of a state of clear consciousness. Criteria for diagnosis were as follows: oriented to place or time less than two times, disoriented to place and time at least once, and never oriented to time, place or person.[15] NP related to acute metabolic disorders (hypoglycemia, ketoacidosis, etc.) were not included in the study.

Statistical analysis: Chi-squared test and Student's *t*-test were used for testing statistical significances. A two-tailed *P*-value was used. A *P*-value of less than 0.05 was considered statistically significant.

Results

Of 1294 patients, 599 (46.29%) had various neurological problems. Frequency of NP was significantly more in patients with type II DM ($P<0.001$) and FCPD ($P<0.05$), while there was no significant difference between type I DM and FCPD patients (Table 1). The type I and II diabetic patients with NP did not differ significantly in their sex distribution and duration of diabetes ($P>0.05$). The difference in their mean age and body weight was highly significant ($P<0.001$), which is obviously consistent with their type of diabetes (Table 2). Type I diabetic patients with NP were older with longer duration of diabetes, compared to those without NP (Table 3). Mean age and duration of diabetes in type II diabetic patients with NP were greater, compared to those without NP ($P<0.001$). The mean fasting blood glucose was higher at the time of admission in the diabetics with NP, compared to those without NP ($P<0.001$). Fewer patients with NP were receiving insulin for the control of hyperglycemia, compared to those without such problems (Table 4).

Different NP encountered in our patient population are depicted in Table 5. Overall, diabetic PNP was the most common neurological problem, with 44.74% of diabetics having it; and constituted 96.66% of all NP. Out of 579 patients with diabetic PNP, 472 (81.52%) patients had distal sensorimotor neuropathy, 43 (7.43%) had subjective sensory neuropathy, 40 (6.91%) had the clinical suggestion of diabetic autonomic neuropathy, 12 (2.07%) had diabetic amyotrophy, 11 (1.90%) had radiculopathy, nine (1.55%) had motor neuropathy, nine (1.55%) had mononeuropathy (with third nerve involvement being the most common) and three (0.52%) patients had mononeuritis multiplex. The study of risk factors for development of diabetic NP revealed that increased age, longer duration of diabetes and poor glycemic control were significant risk factors (Tables 3 and 4). There was an increased incidence of retinopathy, nephropathy and coronary artery disease in patients with diabetic PNP.

During the study period, 33 cases of stroke were seen—29 were ischemic and four were hemorrhagic in origin. The overall frequency of strokes was 2.55% and constituted 5.51% of all NP. The mean age and duration of diabetes in patients with stroke was significantly higher than those without NP (Table 6). The frequency of obesity and coronary artery disease was higher in patients with stroke, compared to patients without NP. Diabetic patients without NP had better glycemic control compared to the stroke group. Surprisingly, there was no difference in the frequency of concomitant hypertension in the two groups.

Parkinsonism was found in nine patients, constituting 1.5% of all NP. Eight of these patients had features suggestive of atherosclerotic brain disease (vascular origin), while one had Parkinson's disease. The overall

TABLE 4. *Comparison between characteristics of type II diabetes mellitus patients with neurological problems (NP) and those without neurological problems.*

Characteristic	Patients with NP (n=545)	Patients without NP (n=542)	Statistical significance
Age (yr)			
Mean±SD	52.07±9.57	47.45±12.87	$P<0.001$ (S)
Range	26-75	27-70	
Sex			
Male:female	286:259	300:242	$P>0.2$ (NS)
Duration of diabetes (yr)			
Mean±SD	6.70±6.04	3.95±4.22	$P<0.01$ (S)
Range	0.02-25	0.02-10	
Obese:non-obese	237:308	222:320	$P>0.2$ (NS)
Fasting blood-glucose*			
Mean±SD (mmol/L)	11.05±4.91	9.08±2.22	$P<0.001$ (S)
Percentage of patients on insulin therapy	44.96	59.59	$P<0.001$ (S)

*Pretreatment in the hospital.

TABLE 5. *Relative frequency of neurological problems in 599* patients with diabetes mellitus.*

Neurological problem	No. of patients	%
Diabetic peripheral neuropathy	579	96.66
Strokes	33	5.51
Ischemic	29	4.84
Hemorrhagic	4	0.67
Parkinson's disease/Parkinsonism	9	1.50
Dementia	6	1.0
Seizure disorders	7	1.17
Myelopathy	2	0.33
Miscellaneous	5	0.83

*75 patients had more than one neurological problem.

frequency of parkinsonism was 0.69%. Among patients with seizure disorder, six had generalized tonic-clonic convulsions, while one had focal convulsions. The overall frequency of seizure disorders was 4.67 per 1000 diabetic patients. Six patients had dementia, predominantly multi-infarct type, with associated cortical atrophy. Frequency of dementia was 0.46% in our diabetic population. Two cases of myelopathy, one compressive and the other noncompressive, were seen. The miscellaneous group comprised one case each of motor neuron disease, pseudobulbar palsy, hypertensive encephalopathy, choreoathetosis and residual poliomyelitis.

Discussion

With the availability of prompt treatment for acute metabolic complications and better control of hyperglycemia, the life span of patients with DM has increased considerably. Long-term complications now constitute a major cause of morbidity in these patients. Complications related to the nervous system are more consistent and least understood. This study has endeavored to provide a comprehensive picture of the pattern of NP in DM from a developing area of the world, where rational management of diabetes continues to be dismal. Even though the results of this study cannot be extrapolated to the general diabetic population, it still serves to provide us with an idea about the frequency of NP in DM. Type II DM was the most common type of diabetes, as is true of other parts of the world,[4] accounting for 84%, while type I diabetes mellitus accounted for 12.91% of the total diabetic population.

Out of 1294 diabetic patients, NP were observed in 599 (46.29%) patients. NP were more common in type II DM, accounting for 50.14%, followed by those in FCPD (32.5%) and type I DM (24.55%). These observations are close to those of Jordan.[18] Hirson et al.[19] found NP in 57% of diabetics; however, the sample size of their study was much smaller. Type I and Type II diabetic patients with NP were older with a longer duration of diabetes as compared to those without NP in our study. Many studies conducted in the past favor these observations.[3,20,21] We did not observe any influence of gender on NP in type II diabetic patients, which is similar to the finding of Young et al.[5] We observed a lesser frequency of NP in type I diabetic males, contrary to the male preponderance reported by Pirart.[20] This is most likely because of social bias against females and the better care offered to males in this part of the world. Poor glycemic control resulted in higher frequency of NP in our patient population. Similar observations have been made by other workers.[20,22] The percentage of patients on insulin therapy was higher in those without NP, indicating that good glycemic control coupled with good compliance in these patients resulted in lesser frequency of NP.

TABLE 6. *Characteristics of type II DM patients with stroke, as compared to those without neurological problems (NP).*

	Diabetics with stroke (n=33)	Diabetics without NP (n=542)	Statistical significance
Age (yr)			
Mean±SD	55.60±7.98	47.45±12.87	*P*<0.001 (S)
Range	40-70	27-70	
Sex			
Male:female	19:14	300:242	*P*>0.50 (NS)
Duration of diabetes (yr)			
Mean±SD	7.8±6.12	3.95±4.22	*P*<0.001 (S)
Range	0.5-25	0.2-10	
Obese (%)	60.60	40.90	*P*<0.05 (S)
Percentage on insulin therapy	42.43	59.59	*P*<0.05 (NS)
Fasting blood-glucose			
Mean±SD(mmol/L)	10.78±4.5	9.08±2.22	*P*<0.05 (S)
Hypertension (%)	60.6	50.0	*P*>0.20 (NS)
Coronary artery disease (%)	30	4.6	*P*<0.001 (S)

The prevalence of diabetic neuropathy has been estimated as high as 62% of diabetics based on subjective complaints, 55% by signs and 100% by nerve conduction studies.[3] We observed that the overall frequency of diabetic PNP was 44.74%, constituting 96.66% of all NP in diabetics. In the United Kingdom, the overall prevalence of diabetic PNP was found to be 28.5% after screening 6487 diabetics in a multicenter study.[5] In Saudi Arabia, the prevalence of diabetic PNP was observed to be 35.9% after screening 1000 diabetics.[4] In comparison to these recent reports, our diabetic population had increased frequency of diabetic PNP, possibly because of illiteracy, ignorance, lack of facilities and economic backwardness in this part of the world. Among 579 diabetic PNP cases, distal sensorimotor neuropathy was the most common (81.5%), followed by subjective sensory neuropathy (7.43%). These findings are consistent with those of Brown et al.[2] Of 10 patients with mononeuropathy, third nerve involvement was the most common, which correlates well with the data in the literature.[23] The study of risk factors for development of diabetic PNP revealed that increased age, longer duration of diabetes and poor glycemic control were significant risk factors. This is in accordance with many studies conducted in the past.[5,20-22] There was an increased frequency of PNP in patients with vascular complications like retinopathy, nephropathy and coronary artery disease. This observation is well supported by Tesfaye et al.[24]

Several large population studies have shown an increase in the prevalence of stroke in the known diabetic population, the undiagnosed diabetic population and those

with glucose intolerance.[6,25] The prevalence of stroke in diabetes varies from 6.1% to 21.1%.[4,6,25] In the present study, stroke was found in 2.55% of diabetics and constituted 5.51% of all NP in diabetic patients. This lesser incidence of strokes found in our study could be because of the fact that diabetic patients presenting with stroke and also those stroke patients with previously undiagnosed diabetes were admitted under the neuroscience division of our Institute and have not been included in our study. The risk of stroke (especially thromboembolic) in diabetics is two to six times that of nondiabetic patients.[6,7,10] Out of our 33 stroke patients, only four were of hemorrhagic origin, while the rest were of ischemic origin. Similar to this, cerebral ischemic and hemorrhagic infarction had been observed in 88% and 8% of diabetic patients with stroke respectively.[9] Age is the biggest risk factor for stroke in the diabetic population.[9,25] We observed that diabetic patients with stroke were significantly older than those without stroke ($P<0.01$). Many studies have shown that diabetic female patients lose the protection of their sex, resulting in higher, or at least equal, prevalence of strokes, compared to male diabetics.[9,26,27] We found equal frequency of stroke in the male as well as the female diabetic population. A large geographic variation in the relative risk of stroke in the diabetic population with respect to sex has been suggested.[9] We observed a significantly increased duration of diabetes in patients with stroke. Evidence also suggests that diabetes of long duration adds to the risk of stroke.[9] In the present study, 60.60% of diabetic patients with stroke were found to be obese. Evidence in literature suggests that obesity is not an independent risk factor for stroke in diabetic patients.[7,9] However, the increased risk of stroke in diabetic patients may be indirectly mediated by obesity through an increase in atherosclerosis, which is a known risk factor for stroke.[6] In the present study, coronary artery disease was observed in 30% of diabetic patients with stroke. Many studies conducted in the past suggested increased prevalence of stroke in patients with vascular complications such as coronary artery disease or peripheral vascular disease.[9,28] We found concomitant hypertension in 66.6% of diabetic patients with stroke, compared to 50% of diabetic patients without NP. In spite of the 40% increased incidence of hypertension in the diabetic population, diabetes and glucose intolerance are independent risk factors for stroke.[25] This could be because of an increased tendency towards atherosclerosis of the carotid arteries in these patients or because of an increased blood viscosity in the diabetic patients.[29] We observed significantly higher mean fasting blood glucose levels in diabetic patients with stroke, compared to those without NP. The Honolulu Heart Program also revealed hyperglycemia to be an important risk factor for stroke in diabetic patients.[8] Hyperglycemia in stroke patients has been shown to result in greater mortality.[7,10]

Parkinsonism was found in nine patients with DM, constituting 1.5% of all NP. The overall frequency of parkinsonism was 0.69%, which is higher than the 162 to 371.5 per 100,000 reported in the literature for the general population.[17,30] Eight of the nine cases of parkinsonism encountered during the study were of the atherosclerotic type. Since arteriosclerosis and atherosclerosis are more common in diabetics,[6,9,29] the increase in the frequency of parkinsonism is expected in this population. The prevalence of seizure disorders in the general population varies from 4.04 to 6.54 per 1000.[15,31] We documented a frequency of 4.67 per 1000 diabetic population. The frequency of dementia in our diabetic population was 0.46%, which is far less than the prevalence of 5% to 50% in the general population of Europe.[32,33] This observed low frequency of dementia may be related to the age structure of the population, as only a small proportion of our diabetic population was more than 65 years old. However, the frequency of dementia in our diabetic population is much higher than that of the general population of the Thugbah community in Saudi Arabia (0.55/1000)[15] and Kelibia in Tunisia (0.29/1000),[31] despite a relatively similar age structure. This may be more a reflection of an increased incidence of cerebral arteriosclerosis in the diabetic population, rather than that of the general population. The odd case of myelopathy, motor neuron disease, pseudobulbar palsy, hypertensive encephalopathy, choreoathetosis and residual poliomyelitis seems to be incidental rather than a direct consequence of DM.

This study suggests that the diabetic population, with increasing age, longer duration of diabetes, and poor glycemic control, are more predisposed to neurological problems, particularly PNP, ischemic stroke and parkinsonism. Better metabolic control and awareness about these problems could result in reduction and/or delay in the onset of these complications.

References

1. Samal KC, Tripathy BB. Diabetic neuropathy. J Assoc Physicians India 1993, Suppl 1:47-56.
2. Brown MJ, Ashbury AK. Diabetic neuropathy. Ann Neurol 1984;15:2-12.
3. Melton JL, Dyck PJ. Epidemiology. In: Dyck PJ, Thomas PK, Asbury AK, Winegrade AI, Porte Jr. D, editors. Diabetic Neuropathy. Philadelphia: WB Saunders, 1987:27-35.
4. Famuyiwa OO, Sulimani RA, Laajam MA, Al-Jasser SJ, Mekki MO. Diabetes mellitus in Saudi Arabia: the clinical pattern and complications in 1000 patients. Ann Saudi Med 1992;12:140-151.
5. Young MJ, Boulton AJM, Macleod AF, William DRR, Sonksen PH. A multicentre study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. Diabetologia 1993;36:150-4.

6. Windebank AJ, McEvoy KM. Diabetes and the nervous system. In: Aminoff MJ, editor. Neurology and general medicine. New York, Churchill Livingston Inc., 1989:273-303.
7. Olsson T, Viitanen M, Asplund K, Eriksson S, Hagg E. Prognosis after stroke in diabetic patients. A controlled prospective study. Diabetologia 1990;33:244-9.
8. Abbott RD, Donahue RP, MacMahon SW, Reed DM, Yano K. Diabetes and the risk of stroke. The Honolulu Heart Program. JAMA 1987;257:949-52.
9. Bell DSH. Stroke in the diabetic patient. Diabetes Care 1994;17:213-9.
10. Pulsinelli WA, Levy DE, Sigsbee B, Scherer P, Plum F. Increased damage after ischemic stroke in patients with hyperglycemia with or without established diabetes mellitus. Am J Med 1983;74:540-4.
11. Diabetes mellitus: report of a WHO Study Group. Tech Rep Ser 1985;727:1-113.
12. Mohan V. Fibrocalculous pancreatic diabetes (FCPD) in India. Int J Diab Dev Countries 1993;13:14-21.
13. Mohan V, Mohan R, Sushella L, Snehalatha C, Bharani G, Mahajan VK, Ramachandran A, Viswanathan M, Kohner EM. Tropical pancreatic diabetes in South India: heterogeneity in clinical and biochemical profile. Diabetologia 1985;28:229-32.
14. Kohner EM, McLeod D, Marshall J. Diabetic eye disease. In: Keen H, Jarrett RJ, editors. Complications of diabetes. 2nd ed. London: Arnold Edward, 1982:19-108.
15. Al-Rajeh S, Bademosio, Ismail H, Awada A, Dawodu A, Al-Freihi H, Assuhaimi S, Borollosi M, Al-Shammasi S. A community survey of neurological disorders in Saudi Arabia: the Thugbah study. Neuroepidemiology 1993;12:164-8.
16. Rajput AH, Offord KP, Beard CM, Kurland LT. Epidemiology of parkinsonism: incidence, classification, and mortality. Ann Neurol 1984;16:278-82.
17. Morgante L, Rocca WA, DiRosa AE, DeDomenico P, Grigoletto F, Meneghini F, et al. Prevalence of Parkinson's disease and other types of parkinsonism: A door-to-door survey in three Sicilian municipalities. Neurology 1992;42:1901-7.
18. Jordan WR. Neuritic manifestations in diabetes mellitus. Arch Int Med 1936;57:307-66.
19. Hirson C, Feinmann EL, Wade HJ. Diabetic neuropathy. Br Med J 1953:1408-12.
20. Pirart J. Diabetes mellitus and its degenerative complications: a prospective study of 4400 patients observed between 1947 and 1973 (Part I). Diabetes Care 1978;1:168-88.
21. Stephenson J, Fuller JH. Microvascular and acute complications in IDDM patients. The EURODIAB IDDM complication study. Diabetologia 1994;37:278-85.
22. Lehtinen JM, Niskanen L, Hyvonen K, Siitonen O, Uusitupu M. Nerve function and its determinants in patients with newly diagnosed type 2 (noninsulin-dependent) diabetes mellitus and in control subjects: a five-year follow-up. Diabetologia 1993;36:68-72.
23. Tarsy D, Freeman R. The nervous system and diabetes In: Kahn CR, Weir GC, editors. Joslin's diabetes mellitus. 13th ed. Philadelphia: Lea and Febiger,1994:794-816.
24. Tesfaye S, Harris N. Jakubowski JJ, Mody C, Wilson RM, Rennie IG, Ward JD. Impaired blood flow and arteriovenous shunting in human diabetic neuropathy a novel technique of nerve photography and fluorescein angiography. Diabetologia 1993;36:1266-74.
25. Barrett-Conner E, Khaw KT. Diabetes mellitus: an independent risk factor for stroke? Am J Epidemiol 1988;128:116-23.
26. Kennel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. JAMA 1979;241:2035-9.
27. Lindergard B, Hillbom. Associations between brain infarction, diabetes, and alcoholism: observations from the Gothenburg population cohort study. Acta Neurol Scand 1987;75:195-200.
28. Tunbridge WMG. Factors contributing to deaths of diabetics under fifty years of age. Lancet 1981;2:569-72.
29. Emara MK, Saadah AM, Tohfa YA, Guindi RT, Gupta RK, Senthilselvan A. The hematocrit value in diabetic patients with ischemic stroke. Diabetes Res 1989;12:189-92.
30. Gudmundsson KR. A clinical survey of parkinsonism in Iceland. Acta Neurol Scan 1967;33:9-61.
31. Romdhane NA, Hamida MB, Mrabet A, Larnaout A, Samoud S, Hamda BA, et al. Prevalence study of neurologic disorders in Kelibia (Tunisia). Neuroepidemiology 1993;12:285-99.
32. Giem P, Beeson WL, Fraser GE. The incidence of dementia and intake of animal products: preliminary findings from the Adventist Health Study. Neuroepidemiology 1993;12:28-36.
33. Launer LJ, Hofman A. Studies on the incidence of dementia: the European perspective. Neuroepidemiology 1992;11:127-34.