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RESEARCH ARTICLE

INCIDENCE OF NEUROLOGICAL COMPLICATION AMONG THE DIABETIC PATIENTS ATTENDING TERTIARY CARE HOSPITAL IN INDIA

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ABSTRACT

World Health Organisation estimates that 422 million adults aged over 18 years were living with diabetes in 2014 and the prevalence of diabetes mellitus has risen dramatically over the past two decades. Diabetes if not controlled causes severe neurological complication that impact significantly on quality of life

Material and method: This was a hospital based cross sectional study, conducted among 616 diabetics. Patients with other potential causes of neurological disorders were excluded from study. After written consent, detailed History and neurological examination of patients was done. Patients were subjected to diabetic neuropathic symptom score (DNS), diabetic neuropathic examination (DNE) score, electro diagnostic studies (NCV) and other necessary investigation for evaluation of various neurological disorders.

Results: Among 616 adult diabetic patients 42.53% were men out of which 93.67 % were Type 2 diabetic with mean age of 56.92 ± 7.96 year. The neurological disorders were present in 73.86%. Type 1 diabetes mellitus patients had higher prevalence of neurological disorders 79.49% compared to type 2 diabetic patients 73.48%.Diabetic neuropathy was the most common neurological complication and was found in 68.01% followed by stroke in 8.6%patients with ischemic (7.46%) > haemorrhagic (1.13%), Isolated cranial neuropathy(1.46%) patients, dementia (1.29%), parkinsonism (1.13%), Transient ischemic attacks (0.97%) and seizure disorder (0.81%).In 26.14% diabetic patients among studied patients there was no neurological complication

Conclusion: Diabetics are prone to develop various neurological complications (73.86 %) and diabetic neuropathy being predominant (68.01%).thus all diabetic patients should undergo periodic neurological examination and all diabetic should be educated about the neurological complication by treating physician about neurological complication

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INTRODUCTION

Diabetes caused 1.5 million deaths in 2012 (Global report on diabetes). The worldwide prevalence of diabetes mellitus has risen dramatically over the past two decades from an estimated 30 million cases in 1985 to 285 million in 2010, with the international diabetes federation projecting that 438 million individuals will have diabetes mellitus by 2030 (Longo *et al.,* 2011). Little was known about diabetes in Kashmir until a recent survey conducted by Zargar *et al* of subjects aged over 40 years in which it was concluded that 1.89% of general population had known diabetes, 4.25% had undiagnosed diabetes and 8.09% had impaired glucose tolerance test, making a total load of abnormal glucose tolerance 14.23% in Kashmir valley (Zargar *et al*., 2000). Diabetes, if not well controlled, may cause blindness, kidney failure, lower limb amputation and several other long-term consequences that impact significantly on quality of life. There are no global estimates of diabetes-related end-stage renal disease, cardiovascular events, lower-extremity amputations or pregnancy complications, though these conditions affect many people living with diabetes. Where data are available mostly

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from high-income countries prevalence, incidence and trends vary hugely between countries (United States Renal Data System, 2014; Moxey *et al.,* 2011). Diabetes is also associated with accelerated atherosclerotic macro vascular disease affecting the arteries that supply the heart, brain and lower extremities. Pathologically, this condition resembles macro vascular disease in nondiabetic patients but it is more extensive and progresses more rapidly (William *et al.,* 2011). The long term neurological complications associated with diabetes include atherothrombotic and lacunar strokes, convulsive disorder in the setting of both hypoglycemia and hyperglycaemia, coma, cranial neuropathies, acute proximal muscle weakness and the most famous complication of diabetic neuropathy (Abbashar Hussein *et al.,* 2009). The risk of developing symptomatic neuropathy in patients without neuropathic symptoms or signs at the time of initial diagnosis of diabetes is estimated to be 4% to 10% by 5 years and up to 50% by 25 years. Stroke is more common in persons with diabetes than in the general population, because of an increased incidence of hypertension and atherosclerosis in the former. Diabetes increases the stroke severity and mortality and predisposes affected persons to deep sub cortical infarctions (Walter *et al.,* 2008). Diabetic patients are prone to develop hypoglycemia and hyperglycaemia and with these the cerebral manifestations like mental obtundation, seizures and coma. Serum hyperosmolality and acidosis probably are important contributing factors in patients with diabetic ketoacidosis. Higher incidence of Parkinson's disease and Alzheimer's has been seen in the diabetic patients (Eva Schernhammer *et al.,* 2011; Geert janBressels *et al.,* 2006).

Objective: To see the incidence of Neurological Complication among the Diabetic Patients attending tertiary care hospital in India

MATERIALS AND METHODS

This was a hospital based cross sectional study, conducted among 616 diabetic patients aged 19 – 70 years attending medical opd and in hospital over period of one year at government medical college srinagerindia from august 2015 to September 2016

EXCLUSION CRITERIA
1 chronic inflammatory polyneuropathy on clinical grounds
2 vitamin B12 deficiency (nutritional anaemia)
3 Hypothyroidism and uraemia
4 Patients with gestational diabetes,
5 secondary causes of hyperglycaemia (i.e., Cushing's syndrome, acromegaly, drugs)

Only patients which gave written consent were included in the study and detailed History regarding the diabetes, duration of diabetes, hypertension, drugs, personal history and other potential causes of neurological was recorded. Detailed Physical examination included general examination like body mass index, blood pressure (both lying and standing) and a detailed neurological examination like assessment of higher mental functions, mini mental status examination i.e. (MMSE), Cranial nerves, motor and sensory examination. Blood glucose at presentation, fasting blood glucose, plasma lipids, complete blood count, Liver and kidney function tests, serum electrolytes, HbA1c were done in each patient. Urine analysis was done in each patient for micro- & macro proteinuria. Brain imaging (CT and MRI) was done in patients who present with hemiplegia, impaired consciousness or convulsion (except those who had documented hypoglycaemia). Neuropathy was evaluated using a diabetic neuropathic symptom score (DNS) (Jan-Willem *et al.,* 2003) and diabetic neuropathic examination (DNE) (Jan-Willem *et al.,* 2000) score. Patients were subjected to electro diagnostic studies (NCV). Stroke was established In patients who presented with 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, abscesses, traumatic cerebral haemorrhages and subdural collections including hematomas along with the imaging evidence.

Transient ischemic attack: The standard definition of TIA required that all neurologic signs and symptoms resolve within 24 hours regardless of whether there is imaging evidence of new permanent brain injury.

Parkinsonism: Was established in those patients who fulfilled the modified core assessment programme for intracerebral transplantation (CAPIT)/Hughe`s diagnostic criteria (Stephen *et al.,* 2003).

Dementia: Those patients who had a mini-mental status examination (MMSE) score of or less were labelled as having dementia (Shaji *et al.,* 2005).

Seizures: Episodes of stereotyped disturbance of cerebral function presenting with impaired consciousness, convulsions, and other motor, sensory, somatosensory, autonomic or psychic features associated automatic behaviour which was not due to an acute cerebral insult, such as head trauma, infections of the central nervous system, stroke, acute or chronic metabolic disturbances such as hypoglycaemia, metabolic acidosis, azotaemia and other endocrinopathies (Cheng *et al.,* 1999).

Diabetic neuropathy symptom (DNS) (Jan-Willem *et al.,* 2003) score

Diabetic neuropathy symptom (DNS) score is a four –item validated score, with high predictive value to screen for PNP (peripheral neuropathy) in diabetes. The four symptoms of unsteadiness in walking, neuropathic pain, paraesthesia and numbness are elicited. The presence of one symptom is scored as 1 point; the maximum score is 4 points. A score of 1 or higher is defined as positive for PNP.

Diabetic neuropathy examination (DNE) (Jan-Willem *et al.,* 2000) score

Diagnosis of parkinsonian disease: Modified Core Assessment Program for Intracerebral Transplantation (CAPIT)/Hughe's Diagnostic Criteria:

RESULTS

The study comprised of 262 (42.53%) men and 354 (57.47%) women Type 2 diabetic patients were 577 in number (93.67%) while type 1 diabetics 39 in number (6.33%). The mean age of studied patients was (56.92 ± 7.96) years, and it was lower in patients with type 1 diabetes (45.10 ± 8.34) years as compared to type 2 diabetic patients in whom it was (57.72 ± 7.28) 65% were from urban while 35 % from rural area, hypertension was found in 67% of studied subjects.49% patients with type1 diabetes had normal blood pressure (i.e., mean BP of < 90 mmHg) while 51% patients had high blood pressure (mean BP more than 90 mmHg).

Table 1. Age and Gender Distribution of Study Subjects

Age (Years)	Male (262)		Female (354)		Total (616)		*P*-value
	n	%	n	%	n	%	
31-40	8	3.05	19	5.37	27	4.38	0.183(NS)
41-50	46	17.56	61	17.23	107	17.37	
51-60	103	39.31	151	42.66	254	41.23	
61-70	105	40.08	123	34.74	228	37.02	
Mean ± SD (Min;Max)	57.42±7.74 (31,69)		56.56±8.11 (36,70)		56.92±7.96 (31,70)		

Table 2. Age Distribution of Study Subjects with different types of diabetes mellitus

Age (Years)	Type-1 DM (n=39)		Type-2 DM (n=577)		Total(616)		*P*-value
	n	%	n	%	n	%	
31-40	9	23.08	18	3.12	27	4.38	< 0.001
41-50	23	58.97	84	14.56	107	17.37	
51-60	5	12.82	249	43.15	254	41.23	
61-70	2	5.13	226	39.17	228	37.02	
Mean ± SD (Min;Max)	45.10±8.34 (31,69)		57.72±7.28 (36,70)		56.92±7.96 (31,70)		

Table 3. Frequency of neurological disorders in different types of diabetes mellitus

Type of diabetes	Neurological disorders Present	Neurological disorders Absent	Total
Type1DM (n=39)	31 (79.49%)	8 (20.51%)	39 (100.0%)
Type2 DM(n=577)	424 (73.48%)	153 (26.52%)	577(100.0%)
Total (n=616)	455 (73.86%)	161 (26.14%)	616 (100%)

Table 4. Prevalence of Neurological Complications in studied Diabetic patients

Neurological Complication	n=number of patients	percentage
Diabetic neuropathy	419	68.01%
Stroke ;(Ischemic: Haemorrhagic)	53	8.6%
Cranial Neuropathy	9	1.46%
Dementia	8	1.29%
Parkinsonism	7	1.13%
Transient ischemic attack	6	0.97%
Seizure disorder	5	0.81%
Normal	161	26.14%

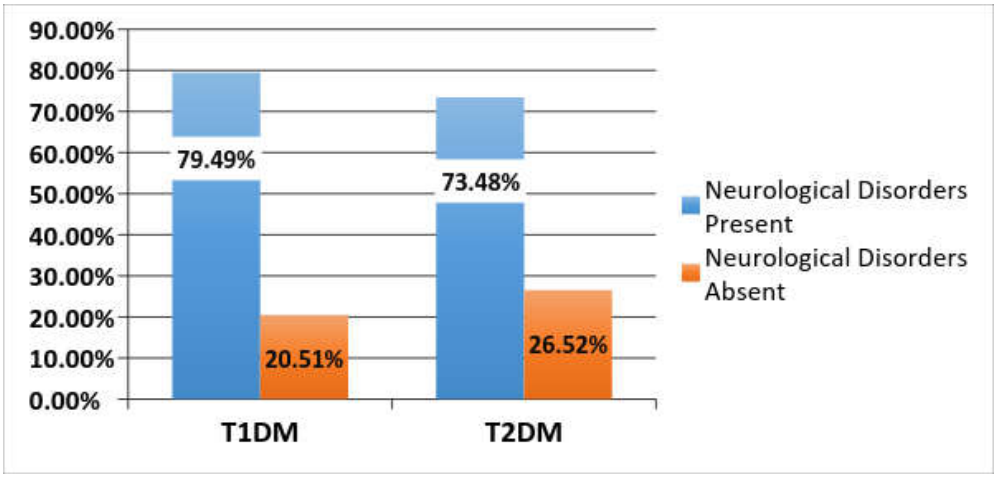

Figure 1. Comparison of neurological disease among patients with type1 and type 2 diabetes mellitus

Among patients with type 2 diabetes, 55% had high blood pressure (mean BP >90 mmHg) while 45% patients had normal blood pressure (mean BP<90mmHg). In our study out of 616 studied diabetic patients, neurological disorders were seen in 455 (73.86%). Patients with type 1 diabetes mellitus had higher prevalence of neurological disorders (79.49) as compared to type 2 diabetic patients (73.48%). Diabetic neuropathy was the predominant neurological complication and was found in 419 (68.01%) studied diabetic patients, 53 diabetic patients had stroke (8.6%) with ischemic(7.46) > haemorrhagic (1.13%), Isolated cranial neuropathy(1.46%) patients, followed by dementia (1.29%), parkinsonism (1.13%), Transient ischemic attacks (0.97%) and seizure disorder (0.81%). In 26.14% diabetic patients no neurological complication was found. Among studied type 1 diabetic patients, peripheral neuropathy was found in (79.48%) and it was higher as compared to type 2 diabetics, (67.24%). It was observed, that with increase in age of patients, percentage of patients with neurological disorders increased. Among diabetic patients in the age group of 31-40 yrs., (18.52%) had neurological complications, percentage of these neurological complications increased to (83%) in patients within the age

group of 60-70 yrs. and the change observed was statistically highly significant. (76%) of diabetic females had neurological disorders as compared to diabetic males (71%) It was observed, that with the increase in mean blood pressure of studied patients, percentage of patients with neurological disorders increased.

DISCUSSION

The study was conducted on 616 adult Kashmiri diabetic patients (type 1 & type 2), comprising of 262 males and 354 females, to evaluate for the neurological complications. It was a hospital based cross sectional study carried out in the department of medicine of SMHS hospital. In our study, overall the prevalence of neurological complications was 73.86% similar to Abbashar Hussein *et al.* (2009) with prevalence of neurological complications among adult Sudanese diabetic patients, and they found that 60% of diabetic patients had neurological manifestations with peripheral sensorimotor neuropathy being the most common (62%) with most of them having diabetes for more than 10 years (65%) as similar to our study with most common neurological disorder been peripheral neuropathy in 68.01%. Besides10% of patients had evidence of cranial nerve lesions. Hemiplegia, paraplegia, epilepsy was noted in 13%, 4% and 2% respectively. In our patients with type 1 diabetes mellitus, prevalence of neurological complications was higher (79.49%) as compared to type 2 diabetics (73.48%), the reason being, that mean disease duration and HbA1c in type 1 diabetics was greater than patients of type 2 diabetes mellitus. Diabetic neuropathy was the predominant neurological disorder observed in studied diabetic patients (68.01%) which was higher than found in other studies, because of long disease duration, poor glycaemic control and less awareness about the disease and its complications. Axonopathy was the most common pattern of neuropathy found in studied diabetic patients (91%) followed by Axonal-demyelination (9%).

The second most common neurological disorder seen in our studied diabetic patients was stroke (8.6%), (ischemic more than haemorrhagic), followed by isolated cranial neuropathy (1.46%), dementia (1.29%), parkinsonism (1.13%) Transient ischemic attack (0.97%) and seizure disorder (0.81%). Out of 64 newly detected diabetic patients 17 patients (26.56%) had neurological complications at presentation, including diabetic neuropathy in 8 patients (12.5%), haemorrhagic stroke in 4 patients (6.25%), ischemic stroke in 4 patients (6.25%) and Transient ischemic attack in 1 patient (1.56%). Diabetic neuropathy was evaluated by using Diabetic Neuropathic Symptom & Diabetic Neuropathy Examination scores and later documented by nerve conduction studies. In our study, female diabetic patients had higher prevalence of neurological disorders (76%) as compared to male diabetic patients (71%).We observed, that with the increase in age of the studied subjects, prevalence of neurological disorders also increased, as age is one of the common non-modifiable risk factors for many diseases. Ab Hamid Zargar *et al*., 2000 analysed data from 1294 patients with diabetes mellitus and concluded that in 46.29% had clinical evidence of one or more neurological problems, predominantly in T2DM (P<0.001). Among these problems, included Peripheral Neuropathy 96.66%, stroke 5.51%, Parkinsonism 1.5%, seizure disorder 1.17% and dementia 1%. The neurological problems were directly related to the duration of diabetes and directly proportional to the fasting blood glucose levels. Neilson *et al* observed neuropathy in 38% of their diabetic patients. Cheng *et al.,* 1999 found diabetic peripheral neuropathy in 33.9% among their Taiwanese patients of diabetic patients. Ratzman *et al*., 1991 and Pirart observed a lower prevalence of diabetic peripheral neuropathy in 6.3% and & 7% respectively in their studies. Ashok *et al.,* 2002 observed a prevalence of neuropathy in 5.4% of their patients with type 2 diabetes at the time of diagnosis. This difference in prevalence of peripheral diabetic neuropathy between their study and ours can be explained because our study used clinical and electrophysiological studies [Diabetic Neuropathy symptom (DNS) score, Diabetic Neuropathy Examination (DNE) score and Nerve Conduction Studies] whereas neuropathy was assessed by Ashok *et al* by using a biothesiometer, which is comparatively less sensitive.

Another factor could be, that our patients attend Diabetes Clinic much later due to less awareness of the disease. Weersuriya *et al.,* 1998 observed that 9.8% of their diabetics had evidence of diabetic neuropathy at the time of diagnosis in their study from Sri Lanka. Franklin *et al.,* 1990 found in their study a prevalence of 27.8% peripheral neuropathy in studied diabetic patients. Brett M Kissela *et al.,* 2005 carried out a population based study and they found that 37-42% of all ischemic strokes in both African Americans and whites are attributable to effects of diabetes alone or in combination of hypertension. Cabezas-Cerrato *et al.,* 1998 in a multiregional cross sectional study among Spanish diabetes patients found that nearly a quarter patients had diabetic peripheral neuropathy and that the prevalence of diabetic peripheral neuropathy increase with age & duration of the disease. Zhaolan Liu *et al*., 2010 found in their study that 6.8% and 17.8% were having cerebrovascular complications and neuropathy respectively. The prevalence of neuropathy was directly proportional to the disease duration (p<=0.01) and glycaemic control. Yu Sun *et al.,* 2011 retrospectively assessed the age and sex specific incidence and relative risk of Parkinson's disease in Taiwanese diabetic patients and they found that diabetes was associated with a significantly elevated risk of PD in all sex and age stratifications except in young women, with the highest hazard ratio (HR) noted for young men aged 21–40 years (2.10 [1.01–4.42]), followed by women aged 41–60 (2.05 [1.82–2.30]) and >60 years (1.65 [1.58–1.73]. Qun Xu *et al.,* 2012 carried a prospective study among older U.S. adults in which out of 288,662 participants of the National Institutes of Health-AARP Diet and Health Study, 1565 participants were included in the analysis to find the relationship between diabetes and future risk of Parkinson's disease (PD) as compared to those without diabetes and they found that PD risk was ~ 40% higher (OR= 1.41 [95% CI 1.20 –1.66]). Further analysis showed that the risk elevation was largely limited to individuals who had diabetes for more than 10 years at the time of baseline survey (1.75 [1.36–2.25]).They concluded that diabetes was associated with a higher future risk of PD and the nature of this association warrants further investigation.

Conclusion

The diabetic patients are prone to develop various neurological complications (73.86 % in our study), with diabetic neuropathy being predominant (68.01% in our study). There should be always high index of suspicion for diagnosis of neurological complication. The complete education should be given to all diabetic patients and caretakers regarding diabetic control and its complication.

Limitation of study

This is hospital based study so true prevalence study is always community based with sample size according to prevalence of diabetes in population .second in the study group it is difficult to exclude other case of neurological problems as most of time there are multifactorial causes of these dosorders.

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