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Original Research Article

Association of diabetic neuropathy with duration of type 2 diabetes mellitus

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Abstract

Diabetic neuropathies (DN) encompass a wide range of nerve abnormalities and are common with prevalence rates reported between 5% and 100% depending on the diagnostic criteria.Diabetic neuropathy is a very problematic complication of diabetes mellitus associated with great morbidity, mortality and a huge economic burden. This study was a Cross sectional non interventional study in the Department of General Medicine, Sree Gokulam Medical College and Research Foundation among Patients with type 2 Diabetes Mellitus admitted in ward and attending OPD in Department of General Medicine, Sree Gokulam Medical College and Research Foundation was done between January 2019 to August 2020. The mean MNSI global score was 9.10, MNSI A mean score was 2.9 and MNSI B mean score in 4.95. The presence of diabetic neuropathy was present in 135 patients (44.8%). Correlation between diabetic neuropathy and age showed that older age groups had significantly higher diabetic neuropathy. Similarly, more duration of diabetes means significantly higher number of neuropathy patients. Hypertension and Dyslipidaemia higher duration showed patients had significantly neuropathy. HbA1C showed higher levels of HbA1C in patients with diabetic neuropathy.

Keywords: Diabetic neuropathy, Duration,Type 2 diabetes mellitus

Introduction

Diabetes is a serious, chronic disease that occurs either when the pancreas does not produce enough insulin[1] or when the body cannot effectively use the insulin it produces [2]. In public health diabetes mellitus has severe microvascular and macrovascular complications. There are 3 key types of diabetes mellitus (DM): Type 1 DM occurs from the failure of pancreas to yield sufficient insulin. This form was previously denoted as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes", its exact cause is not known. Type 2 Diabetes Mellitus (T2DM) begins with insulin resistance, a condition in which cells fail to respond to insulin properly [1]. As the disease progresses a lack of insulin may also develop [2]. This form was previously referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". Gestational diabetes, which is a form of glucose intolerance that affects some

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women during pregnancy a group of other types of diabetes caused by specific genetic defects of beta-cell function or insulin action, diseases of the pancreas, or drugs or chemicals. As a consequence of population's demographic changes, we are witnessing an increase in the proportion of persons of 60 years or older in parallel with a decline in the proportion of the young, such that by 2050 it is expected that the proportion of elderly persons will have risen from 15% up to 25%. This demographic shift will have a direct impact on the epidemiology of chronic, non-transmissible diseases, including type 2 diabetes mellitus (T2DM). Now a days the prevalence of T2DM is approximated at 382 million cases being expected to affect 592 million people by 2035. As T2DM is predominantly more prevalent in ageing population this premise is creating a major health burden [3]. Although the burden of diabetes is often described in terms of its impact on working age adults, diabetes in older adults is linked to higher mortality, reduced functional status and increased risk of institutionalization [4]. Older adults with diabetes are at substantial risk for both acute and chronic microvascular and cardiovascular complications of the disease.

Diabetic neuropathies (DN) encompass a wide range of nerve abnormalities and are common with prevalence rates reported between 5% and 100% depending on the diagnostic criteria. [5, 6, 7] Diabetic neuropathy is a very problematic complication of diabetes mellitus associated with great morbidity, mortality and a huge economic burden. Diabetic neuropathy consists of a family of neurological syndromes that affect specific regions of the nervous system, occurring in both Type 1 and Type 2 diabetes mellitus and also in acquired diabetes [8]. Its occurrence is explained by a multifactorial aetiology that includes up-regulation of the polyol pathway, functional and structural microvascular disturbances, nervous and ganglionic hypoxia, increased oxidative stress, impairment in glycosylation of axonal and microvascular proteins and impaired trophic factors required for peripheral nerves and their ganglia [9]. The San Antonio Convention divides neurological disturbances related to diabetes mellitus into subclinical neuropathy, assessed by anomalies in electrodiagnostic and quantitative sensory testing and diffuse clinical neuropathy involving distal sensorimotor and autonomic dysfunction and focal syndromes [10].

Neuropathy is associated with several risk factors, such as raised triglyceride levels, body mass index, smoking, hypertension [11] and diabetic microvascular [12] and macrovascular injuries [13]. Lack of insulin or C-peptide or both also promotes severe axonal atrophy and loss of axons [14]. Mismanagement of this complication can further lead to foot ulceration; a harbinger of gangrenous limb loss. According to the diabetic wound classification system proposed by Armstrong, *et al*., risk of amputation is increased by 1.7 times in the case of diabetic neuropathy, 12 times in case of deformity and 36 times if there is a history of previous ulceration [15]. Progression of diabetes mellitus and associated complications can be controlled with good glycaemic control by the patient. According to the Diabetes Control and Complications Trial Research Group, intensive therapeutic management of insulin-dependent diabetes reduces the onset and progression of diabetic complications by 35-70% [16]. There is overwhelming evidence that early insulin therapy provides neuroprotective effects in patients with Type 2 diabetes who have diminished insulin secretion [17]. Distal symmetrical neuropathy is the most common form of DN [18]. The duration and severity of hyperglycaemia, presence of dyslipidaemia, hypertension and smoking are major risk factors for the development of diabetic polyneuropathy [19]. Therefore this study was done to assess whether duration of diabetes is an independent factor for the occurrence of DN and to evaluate the relationship between the presence and severity of DN and the diabetes duration and blood glucose level.

ISSN 2515-8260 Volume 09, Issue 06, 2022

Materials and Methods

This study was a Cross sectional non interventional study in the Department of General Medicine, Sree Gokulam Medical College and Research Foundation among Patients with type 2 Diabetes Mellitus admitted in ward and attending OPD in Department of General Medicine, Sree Gokulam Medical College and Research Foundation was done between January 2019 to August 2020.

Inclusion criteria

Were Patients diagnosed with diabetes mellitus, history of/currently symptomatic with DN (as defined by clinical symptoms and MNSI screening tool), able to provide informed consent for participating in study, Able to provide accurate medical history data. No reported/diagnosed/documented history of non DN. No major cardiovascular events (as per hicks 2014 criteria) 3 months preceding study.

Exclusion criteria

Were patients with inability to provide informed consent, Inability to provide accurate anamnestic medical history data. Prior history of non-DN, Presence of major cardiovascular events (according to Hicks 2014 criteria), 3 months prior to screening, Presence of any other condition which in the investigator`s opinion could lead to biases in study results.
With a Sample size of 300. Sampling of Patients who matched the inclusion and exclusion criteria were selected by using consecutive sampling technique.
After approval from the Institutional ethics committee and obtaining informed written informed consent from each patient, History, Physical examination, as per the proforma was done in all patients. Age of the patients (in years), duration of type 2 diabetes mellitus (in years), and prior history of smoking and alcohol consumption will be assessed. Severity of DN was done by evaluation of clinical symptoms. All patients will have their HbA1c, lipid profile and BMI measured. Also all patients will have their waist circumference measured, normal was defined as below 94 cms for men and below 80 cms for women. Hypertension was defined as resting blood pressure above 140 mmHg (systolic) and/or above 90 mm Hg (diastolic). Presence and severity of chronic kidney disease was diagnosed according to Kidney Disease: Improving Global Outcomes 2012 guidelines. Autonomic neuropathy was assessed using the presence of orthostatic hypotension, defined as fall in blood pressure in response to postural changes (more than 20 mm Hg for systolic or more than 10 mm Hg for diastolic blood pressure). Michigan Neuropathy Screening Instrument (MNSI) is a score instrument designed for diagnosis and severity evaluation of DN, which contains a patient's symptom questionnaire and clinical assessment tool. Positive for overt neuropathy was defined as presence of ONE out of the following criteria: a global score ≥9.5, questionnaire score ≥7, or clinical score ≥2.5. Higher score is associated with more severe neuropathy. The study variables are Age (in years), duration of diabetes mellitus type 2 (in years), glycated Hb (as %), BMI (kg/m2), waist circumference exceed (cm), total cholesterol (mg/dl), HDL cholesterol (mg/dl), LDL cholesterol (mg/dl), triglycerides (mg/dl), male gender, presence of hypertension, smoking, alcohol consumption, chronic kidney disease, retinopathy. Data analysis after collecting the data, it will be entered to a computer and was analysed by SPSS trial version 22 software. The necessary statistical tables were constructed along with charts and diagrams. Correlation coefficient was computed to find out the relationship between age and DN score. Impact of other factors was assessed using regression analysis.

ISSN 2515-8260 Volume 09, Issue 06, 2022

Results

Table 1

Diabetic neuropathy and its comparison	Diabetic Neuropathy		
Age in years	**DN absent n (%)**	**DN present n (%)**	**Chi-square**
31 to 40 years	38 (23.0)	00 (00.0)	p value: <0.001
41 to 50 years	53 (32.0)	00 (00.0)	
51 to 60 years	58 (35.0)	00 (00.0)	
61 to 70 years	04 (10.0)	26 (19.0)	
71 to 80 years	00 (00.0)	54 (40.1)	
81 to 90 years	00 (00.0)	55 (40.9)	
Diabetes duration	**DN absent n (%)**	**DN present n (%)**	**Chi-square**
31 to 40 years	00 (00.0)	55 (40.5)	p value: <0.001
21 to 30 years	00 (00.0)	15 (11.5)	
11 to 20 years	43 (26.0)	64 (48.0)	
6 to 10 years	22 (13.3)	00 (00.0)	
1 to 5 years	71 (42.9)	00 (00.0)	
< 1 year	30 (17.8)	00 (00.0)	
Hypertension duration	**DN absent n (%)**	**DN present n (%)**	**Chi-square**
1 to 5 years	11 (06.6)	07 (2.60)	p value: <0.001
6 to 10 years	01 (0.60)	06 (2.20)	
11 to 20 years	07 (4.20)	72 (26.8)	
21 to 30 years	04 (2.10)	10 (3.70)	
31 to 40 years	00 (00.0)	50 (18.6)	
DLP duration	**DN absent n (%)**	**DN present n (%)**	**Chi-square**
> 20 years	00 (00.0)	02 (1.50)	p value: <0.001
11 to 20 years	00 (00.0)	06 (4.10)	
6 to 10 years	00 (00.0)	16 (11.9)	
1 to 5 years	00 (00.0)	24 (17.8)	
HbA1C	**DN absent n (%)**	**DN present n (%)**	**Chi-square**
Normal HbA1c	76	40	p value: 0.004
High HbA1c	90	95	

Correlation between diabetic neuropathy and age showed that older age groups had significantly higher diabetic neuropathy. Similarly, more duration of diabetes means significantly higher number of neuropathy patients. Hypertension and Dyslipidaemia higher duration showed patients had significantly neuropathy. HbA1C showed higher levels of HbA1C in patients with diabetic neuropathy

Dyslipidaemia Profile

Duration of dyslipidaemia showed most had it for 1 to 5 years (8%), followed by 6 to 10 years (5.3%). The mean duration of dyslipidaemia was 6.79 years.

Table 2

Dyslipidaemia profile		
Duration of Dyslipidaemia	**n**	**%**
No DLP	253	84.2
> 20 years	2	0.7
11 to 20 years	5	1.8
6 to 10 years	16	5.3
1 to 5 years	24	8.0

ISSN 2515-8260 Volume 09, Issue 06, 2022

Mean duration 6.79 ± 5.0 years

Correlation coefficient showed higher correlation for age and diabetes with MNSI score, there was lower correlation with hypertension durations and dyslipidaemia duration with MNSI score.

Table 3

Correlation of MNSI and other Variables	Correlation coefficient	R^2 value
Age in years	0.886	0.786
Diabetes duration	0.895	0.801
Hypertension duration	0.565	0.319
DLP duration	0.362	0.131

The mean MNSI global score was 9.10, MNSI A mean score was 2.9 and MNSI B mean score in 4.95. The presence of diabetic neuropathy was present in135 patients (44.8%)

Table 4

MNSI	Mean	S.D
MNSI A	2.90	1.9
MNSI B	4.95	1.0
MNSI Global	9.10	2.6
Diabetic Neuropathy	**n**	**%**
MNSI Global Score ≥ 9.5 (DN present)	135	44.8
MNSI Global Score ≤ 9.5 (DN absent)	165	55.2

Hypertension Profile

Duration of hypertension showed that 205 patients were not having hypertension (68.3%) and rest were having hypertension, in them most had hypertension for 11 to 20 years (14.3%) and 8.3% had hypertension for 31 to 40 years. The mean duration was 19.65 years.

Table 5

Hypertension profile		
Duration of Hypertension	**n**	**%**
No Hypertension	205	68.3
1 to 5 years	14	04.8
6 to 10 years	04	01.3
11 to 20 years	43	14.3
21 to 30 years	09	02.8
31 to 40 years	25	08.3
Mean duration 19.65 ± 10.9 years		

ISSN 2515-8260 Volume 09, Issue 06, 2022

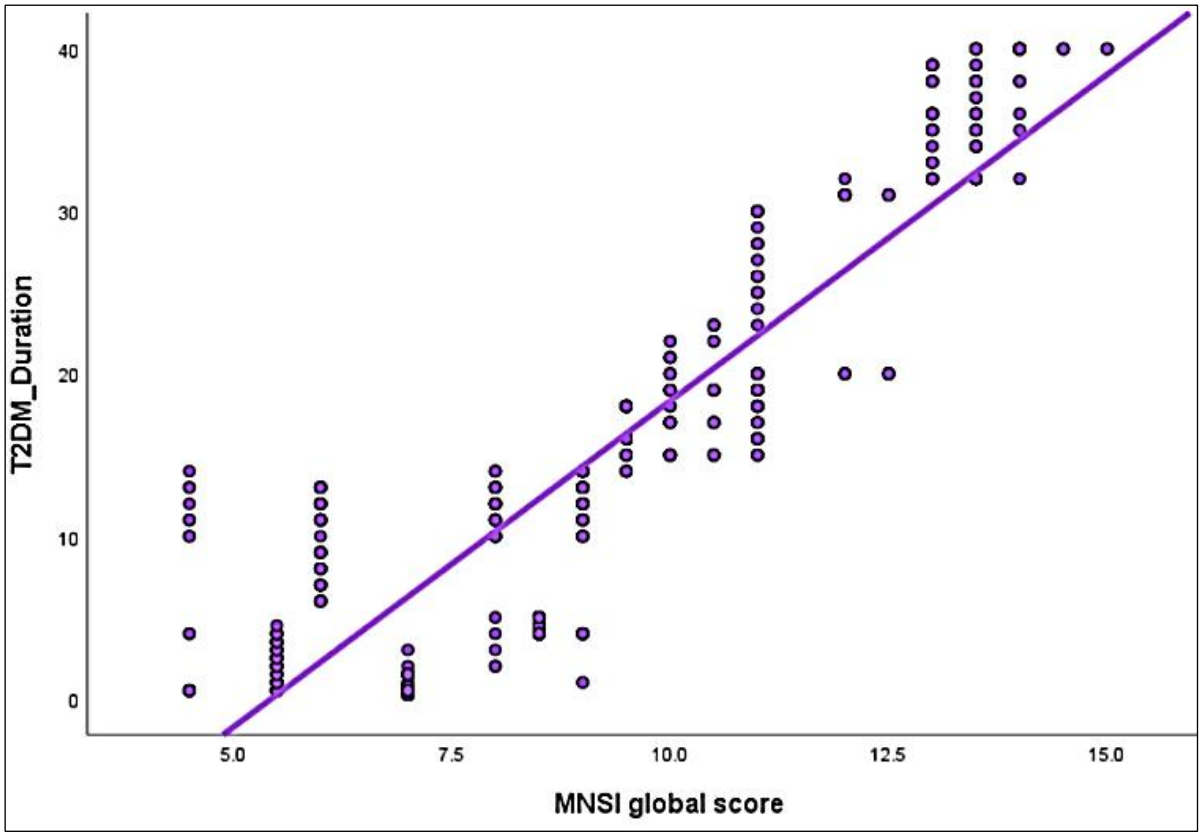

Fig 1: Correlation between Diabetic Neuropathy and T2DM duration

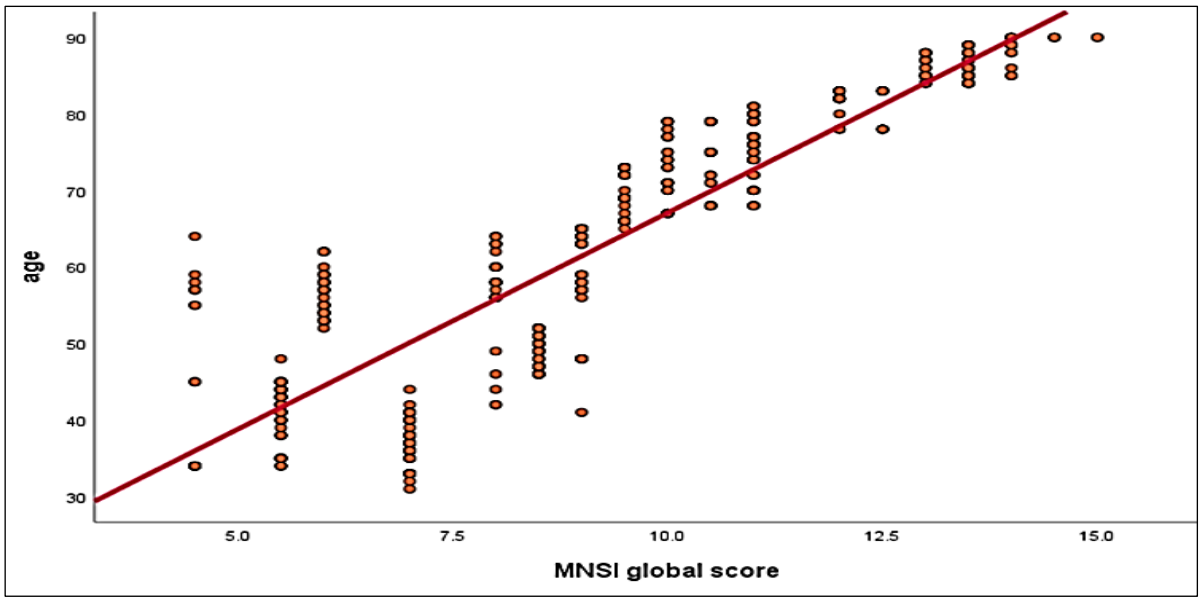

Fig 2: Correlation between Diabetic Neuropathy and Age

Discussion

A hospital-based cross-sectional non-interventional study was done on patients with type 2 Diabetes Mellitus admitted in ward. In our study correlation between diabetic neuropathy and age showed that older age groups had significantly higher diabetic neuropathy. Similarly, more duration of diabetes means significantly higher number of neuropathy patients. Hypertension and dyslipidaemia higher duration showed patients had significantly neuropathy. This was similar to reviewed literature where a long duration of diabetes and poor glycaemic control is associated with increased production of glycosylation end products,

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metabolic derangements, endothelial injury, and oxidative products [20, 21]. Oguejiofor, *et al*. found a lower prevalence of polyneuropathy in those with duration of DM < 5 years and highest in those with a duration of DM > 15 years [22]. A large study in the UK showed that neuropathy was present in as many as 36% people with duration of diabetes greater than 10 years as compared to 20% when duration of diabetes was five years [7]. Sensory neuropathy and the extent of skin denervation also increases with duration of diabetes [23]. The association between the duration of diabetes mellitus and neuropathy was also evident in a research study on the epidemiology of diabetic complications [24] As in published literature, we found that diabetic neuropathy is more common among elderly people and during its evolution is accompanied by an account of complications, which is why DN should be diagnosed and treated earlier [25]. Like in other studies, we observed that the influence of age persists even after adjusting for other very important risk factors like glycaemic control or diabetes duration. It is known that complications of T2DM are a consequence of a long-time poor glycaemic control, this being the reason why in many studies the presence and severity of diabetic neuropathy and other T2DM complications is described as being associated with a longer diabetes duration [26].

In our present study HbA1C showed higher levels of HbA1C in patients with diabetic neuropathy. Patients with an HbA1c > 6.5% were 16.9 times more likely to develop neuropathy. The role of poor glycaemic control and chronic hyperglycaemia as a risk factor for diabetic neuropathy has also been established in several longitudinal studies by Dyck PJ *et al*. [27] and Adler AI *et al*. [28] The severity of hyperglycaemia and abnormal glycaemic hemoglobin levels considerably affect the results of the sensory and motor NCS tests [29]. This might be due to the fact that abnormal levels of HbA1c are positively associated with neuromuscular jitters and fibre densities [30]. These variations in HbA1c are also associated with other diabetic complications as evident in a multicentre study, which has established variation in HbA1C to be an important risk factor of diabetic retinopathy [31]. Tight blood glucose control significantly reduced the risk of microvascular complications in the Diabetes Control and Complications Trial (DCCT), which showed that intensive insulin therapy reduced incidence of albuminuria by 54% and decreased mean risk of retinopathy by 76% [17]. Reviewed studies also recommend a target HbA1c as close to normal as possible, which provides improved outcomes. The UKPDS showed that HbA1c below 6% had the lowest risk for diabetes-related complications and for every 1% decrease in the mean HbA1c, there was a 37% decrease in microvascular complications [32]. Patients in the UKPDS who were intensively treated for diabetes and maintained an HbA1c below 7% had a 12% decrease in diabetes-related microvascular events.
The mean MNSI global score was 9.10, MNSI A mean score was 2.9 and MNSI B mean score in 4.95. The presence of diabetic neuropathy was present in 135 patients (44.8%). Correlation between diabetic neuropathy and age showed that older age groups had significantly higher diabetic neuropathy. Similarly, more duration of diabetes means significantly higher number of neuropathy patients. Hypertension and Dyslipidaemia higher duration showed patients had significantly neuropathy. HbA1C showed higher levels of HbA1C in patients with diabetic neuropathy.

Conclusion

The presence of diabetic neuropathy was significantly observed among older age groups. The duration of T2DM showed higher the duration of diabetes there were significantly more chance of diabetes neuropathy. The poor glycaemic control also had significant association with presence of diabetes neuropathy. The presence of hypertension and dyslipidaemia also had significant association with presence of diabetes neuropathy.

ISSN 2515-8260 Volume 09, Issue 06, 2022

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