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Correlation of diabetic peripheral neuropathy with peripapillary retinal nerve fibre layer thickness in patients with type 2 diabetes mellitus

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Abstract
Context: To correlate Diabetic peripheral neuropathy with peripapillary retinal nerve fibre layer thickness in patients with type2 diabetes mellitus.
Aims: To correlate peripapillary retinal nerve fibre layer thickness of DM patients with Diabetic peripheral neuropathy.
Settings and Design: Cross-sectional analytical study.
Methods and Material: This hospital based cross-sectional study included patients attending the outpatient department of our institution with the following criteria, 50 subjects diagnosed with type 2 diabetes mellitus were included.
Results: It showed a significant (0.014) thinning of global peripapillary retinal nerve fibre layer thickness in left eyes with diabetic peripheral neuropathy positive comparison to no diabetic peripheral neuropathy patients. There was no significant difference in the right eye.
Conclusions: Individuals with diabetic peripheral neuropathy showed significant thinning in peripapillary retinal nerve fibre thickness. This may suggest a common pathway of neurodegeneration for both these complication. Peripapillary retinal nerve fibre layer thickness can be used as a means of screening for diabetic peripheral neuropathy to improve the efficiency of clinical diabetic peripheral neuropathy detection.

Keywords: A significant association present between DR, DPN and their severities. The neurodegenerative changes are in parallel to DPN in the course of DM. Peripapillary RNFL thickness can be used as a means of screening for DPN to improve the efficiency of clinical DPN detection

Introduction

Type 2 Diabetes mellitus (DM) is a multifactorial metabolic disease characterized by sustained hyperglycaemia leading to long term complications such as Diabetic retinopathy (DR), nephropathy and diabetic peripheral neuropathy (DPN) and other vascular complications.

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycaemia [1]. The prevalence of type 2 DM in world was 9.3% [2] and in India was between 10.9 and 14.2% in 2019 [3].

DPN is the most common component in the causal sequelae to foot ulceration. The prevalence of DPN in DM estimates to 50% as studied in the previous literature [4]. Pfeiffer *et al*., studied that among 7.5% of the participants, 45% developed DPN after 25 years of follow up [5]. Abbott *et al* studied that a large cohort of people with DPN developed diabetic foot after one year.

Since the gold standard diagnostic tool in the diagnosis is Nerve conduction studies (NCS) and Electro-diagnostic tests such as Electro Myography (EMG) [6], since they cannot be used for the routine diagnosis due to availability issues, we used an alternate method and diagnosed with the index test Michigan neuropathy screening instrument (MNSI) [7].

Retinal neurodegenerative changes in DR have been shown to precede micro vascular changes in some previous studies, also known as Diabetic retinal neurodegeneration (DRN) caused by neuronal apoptosis and glial cell activation resulting in thinning of PRNFLT even in the absence of DR progression.

DPN ranks third after the micro vascular disease and nephropathy in lifetime expenditures and is a large burden in a developing country like India.

The cost of long term treatment and dependency becomes much heavier, when the patient with DPN progress to diabetic foot and it's complications.

In a study by Rehna Rasheed *et al*. [17], studied that there was a significant association of DPN and DR, and early changes in inner retinal layers of diabetic patients without microvascular changes of DR and these neurodegenerative changes parallel with DPN in the course of DM.

Thus, the early screening and diagnosis of DPN helps in the early intervention in the form of enhanced glucose control and neuro-protective agents, thus preventing the patient landing in devastating complications of diabetic foot leading to foot amputation. Hence, this study was conducted to correlate DPN with peripapillary RNFL thickness in type 2 diabetics.

Subjects and Methods

This cross-sectional study was carried out between February 2021 and august 2022, after approval from institutional ethical committee and taking written informed consent from patients. Patients of either gender aged 41-60 years, either normal individuals or with the diagnosis of type2 DM were included.

Patients with glaucoma, proliferative DR(PDR),congenital optic disc anomalies, optic neuropathies, oculr trauma, previous retinal laser photocoagulation, media opacities, high refractive errors >±6D, and poor OCT strength <6 were excluded. Demographic data of study population was acquired. Patients fulfilling the above criteria were included.

All patients underwent a comprehensive ophthalmic examination with measurement of best corrected visual acuity (BCVA), anterior and posterior segment examination with staging of DR (According to ETDRS classification) [9].

Peripapillary RNFL thickness measurements were taken using Cirrhus HD OCT (Carl Zeiss Meditec) after pupillary dilatation with 0.8%Tropicamide + 5%phenylephrine eye drops. Global as well as mean peripapillary RNFL thickness of all four quadrants was taken.

SPSS (version 17, IBM) was used for statistical analysis. Descriptive statistics (mean± SD) for quantitative values (age, RNFL) and frequencies with % for qualitative variables were used to describe the data. Quantitative variables were compared between the groups using one way ANOVA test. A p value of ≤0.05 was considered statistical significant.

Screening for DPN – Index test Michigan Neuropathy Screening Instrument (MNSI) [10]

- Q (15)- Sensory symptoms, cramps, muscle weakness, foot ulcer;
- E-Foot appearance, ankle reflex 128 HZ tuning fork.

DPN + DPN-
Q>7;E>2 Q<7;E<2

Results

1. Patient characteristics

In our study, out of 50 diabetic's patients, there were 26 males and 24 females. Mean age was 54.38±6.12 years.

There were 15 patients (66% of the patients were in age group 56-60 years) who had DPN, and 35 patients who had no DPN. There was no difference in gender distribution.

DPN positive patients had duration of DM > 10 years and HbA1c > 7%.

The age of the patients in this study ranged from 41 to 60 years and the age-wise distribution of patients is as shown in table 1.

We compared the BCVA in log MAR among the normal subjects with the DM groups and found a significant reduction of BCVA in DPN positive patients compared to no DPN patients in both the eyes.

2. Correlation of global peripapillary RNFL thickness with DPN

As depicted in table 2, there was a significant thinning of peripapillary RNFL thickness in patients where DPN was present in the left eyes in comparison to no DPN patients, similar to the study by Rehna Rasheed *et al*. [2] and Cirous Dehghani *et al*. [3].

Discussion

Age and gender

Our study population age group ranged from 41 to 60 years. The study included 26 males and 24 females. As per the Barbados Eye Study [11] most of the diabetic patients were in the age group of 50-64 years, which is similar to our study. Also in a study by Rania, *et al.* [12] majority of the DM patients were in the age group of 40-59 years. The prevalence of vision threatening DR were most among the age group of 50-64 years as well.

Among the 50 diabetic patients, 26 (52%) were females and 24(48%) were males.

As per the previous studies such as Barbados Eye Study, Barbados conducted from 1988-1992 show that females were prone for diabetes. Also in a study by Irini Chatzivalli [13] *et al*. females were more, but in contradiction males were more in the study conducted by Rania *et al*.

However, in our study we had almost equal number of males and females.

BCVA in DM

There was a significant reduction of BCVA in DPN positive patints compared to no DPN patients in both the eyes. Our study results were similar to the study by Jin li *et al.* [14] and is correlated to micro vascular ischaemia and retinal neurodegeneration in DR, greater levels of DR severity corresponded to worse vision.

Correlation of global peripapillary RNFL thickness with DPN

In our study, we found significant thinning of peripapillary RNFL thickness in both the eyes of DPN positive patients in comparison to no DPN patients. Peripapillary RNFL thinning diabetics is explained Diabetic retinal neurodegeneration. DRN can be attributed to various factors resulting in neuronal degeneration from metabolic derangements, reactive gliosis, glutamate excitotoxicity and nerve fibre layer and ganglion cell apoptosis, which results in thinning of peripapillary RNFL thickness.

DPN mostly affects the lower limbs and the feet, and in some cases upper limb also affected. It is a chronic, symmetrical condition affecting multiple nerves. DPN of the limbs increases with increasing age and DM duration. It is associated with suboptimal glycaemic control and obesity following a stocking glove pattern. It often starts at the distal end of the long nerves and moves proximally. All the patients with DM (both types 1 and 2) should undergo DPN screening.

Our study results were similar to the study by Rehna Rasheed *et al*, [16] studied that there was a significant association of DPN and DR, and early changes in inner retinal layers of diabetic patients without microvascular changes of DR and these neurodegenerative changes parallel with DPN in the course of DM.

As recommended by the 1988 consensus statement from the San Antonio conference on Diabetic neuropathy, for the diagnosis and classification of DPN multiple tests, quantitative sensory testing and autonomic function testing is required.

Table 1: Demographic data

Characteristics	DPN +	DPN-
1. Age		
41-45	-	12
46-50	2	10
51-55	3	10
56-60	10	3
2. Gender		
Male	8	18
Female	7	17
3.BCVA	-	-
< 6/60	-	-
6/60-6/18	3	-
> 6/12	12	35
4. Duration of DM (years)	10.36	6.1
5. HbA1c		
< 7%	13	25
> 7%	2	10

Table 2: Comparison of global PRNFLT with DPN

Global PRNFLT	DPN +	DPN -	t	P
RE mean	85.76	84	1.31	0.2
LE mean	82.79	88.22	2.55	0.014*

Conclusion

Individuals with DPN showed significant reduction in peripapillary RNFL thickness. This may suggest a common pathway of neurodegeneration for both these complication.

- There is a significant association between DR, DPN and their severities. The neurodegenerative changes are in parallel to DPN in the course of DM.
- Peripapillary RNFL thickness can be used as a means of screening for DPN to improve the efficiency of clinical DPN detection.

DPN screening in the early diagnosed DR patients helps to know patients at the earliest and thus, helpful in early therapeutic approach in the prevention of diabetic foot complications.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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