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RETINAL NERVE FIBER LAYER THICKNESS ASSOCIATED WITH SEVERITY OF DIABETIC PERIPHERAL NEUROPATHY IN DIABETES MELLITUS TYPE 2

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Abstract

Introduction**:** *To identify whether the Retinal Nerve Fiber Layer is useful in detecting severity of peripheral neurodegeneration in diabetic patients*

Methods: *A cross-sectional study was conducted. 36 people were enrolled in this study which is divided into two groups. 18 people with type 2 diabetes mellitus (DM) with Diabetic Peripheral Neuropathy (DPN) and 18 people with type 2 DM non-DPN. All subjects were 40-60 years old, and the best corrected visual acuity was better than 0,2 logMAR. An Optical Coherence Tomography (OCT) examination was carried out to determine the Retinal Nerve Fiber Layer (RNFL) thickness, an Electroneuromyography (ENMG) examination and DNS-Ina Score was applied to establish a diagnosis of DPN. Data were analyzed with independent T-test and Spearman correlation analysis.*

Results**:** *The average RNFL thickness in the DM with DPN was thinner than the RNFL thickness in the DM non-DPN group (100.22 ± 38; vs 102.61±9.11; p 0.444). At temporal quadrant and nasal quadrant, RNFL was also thinner in DM DPN group than DM non-DPN group (71.78±12.21, vs 76.33 ± 8.53, p 0.203; and 75.11±11.38 vs 77.39 ± 14, p 0.596). Sural and tibial amplitude (14.44±2.87 and 6.85± 4.98) , were the most significant predictor values in determining the severity of DPN (p=0.000). Average, temporal, and nasal RNFL thinning has an inverse association with DPN severity (r=-0,285; -0,258;and -0,126)*

Conclusion: *RNFL was thinner at average, temporal, nasal quadrant in the DM group with DPN compared to DM non-DPN group. RNFL thickness has an inverse association with the severity of the DPN although they were not statistically significant.*

Keywords: Diabetes Mellitus, Diabetic Peripheral Neuropathy, Retinal Nerve Fiber Layer **Cite This Article**: PUTRI, Mutiara Kristiani et al. RETINAL NERVE FIBER LAYER THICKNESS ASSOCIATED WITH SEVERITY OF DIABETIC PERIPHERAL NEUROPATHY IN DIABETES MELLITUS TYPE 2. **International Journal of Retina**, [S.l.], v. 8, n. 1, p. 26, mar. 2025. ISSN 2614-8536. Available at: <https://www.ijretina.com/index.php/ijretina/article/view/320>. Date accessed: 05 mar. 2025. doi: https://doi.org/10.35479/ijretina.2025.vol008.iss001.320.

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INTRODUCTION

Diabetes Mellitus is a long-term metabolic disorder characterized by hyperglycemia caused by insulin insufficiency or resistance. Diabetes Mellitus is becoming more common over the world. According to the International Diabetes Federation (IDF), there will be 415 million diabetes patients globally in 2015. In 2017, there were 10.3 million Diabetes Mellitus patients in Indonesia, with a projected increase to 16.7 million by 2045. Diabetes is known to produce a variety of microvascular problems, including retinopathy, neuropathy, and nephropathy [1,2]

Diabetic retinopathy is a microvascular complication of the eye caused by the most frequent type of diabetes mellitus; this complication can result in permanent vision loss. Diabetic retinopathy is a known cause of blindness in persons of working age. According to statistics, 93 million individuals worldwide suffer from diabetic retinopathy, with the number expected to rise to 224 million by 2040. Early detection and screening are critical components in the prevention and treatment of this disease.[3] Diabetic peripheral neuropathy (DPN) is another microvascular consequence that affects 30-50% of diabetic patients. It is caused by hyperglycemia and microvascular dysfunction, which causes nerve ischemia. Diabetes. The Retinal Nerve Fiber Layer (RNFL) can be assessed using Optical Coherence Tomography (OCT), which is impacted by diabetes and is associated with the development of Diabetic Peripheral Neuropathy (DPN).[4]

The relationship between these two issues is particularly important for various reasons, including pathophysiological and clinical involvement. Many studies have focused on vascular changes associated with this condition, but several recent studies have discovered evidence that neuronal changes occur prior to clinical vascular abnormalities. It is also stated that peripheral neuropathy can cause changes in the thickness of the retinal nerve fiber layer (RNFL). This can happened even before the retina suffers microvascular injury. The retinal nerve fiber layer (RNFL) may be one of the objective indicators of a neurodegenerative state similar to that occurring in patients with diabetic peripheral neuropathy based on this evidence, which suggests that thinning of the RNFL occurs prior to vascular changes. This study also explores the understanding of the underlying pathophysiological relationship between these two microvascular problems and describes the relationship between diabetic retinopathy and diabetic peripheral neuropathy.[5] Therefore, the purpose of this study was to determine the relationship between retinal nerve fiber layer thickness and the severity of diabetic peripheral neuropathy in type 2 diabetes mellitus patients

METHODS

A cross-sectional study was used in this study. The data for this study was collected from the Endocrinology, Neurology, and Ophthalmology Polyclinics at Dr. Saiful Anwar General Hospital from March to December 2022. The participants in this study were Type 2 Diabetes Mellitus outpatients at the Endocrinology and Neurology polyclinic of Dr. Saiful Anwar General Hospital (Diagnosed by endocrinologist with HbA1c > 6.5%). All patients are 40-60 years old age, no other ocular or systemic disease detected that can caused retinopathy and other caused of peripheral neuropathy. According to the estimation results, this study is more appropriate to use the Lemeshow formula, which is adjusted to the study design and no treatment is performed in each group, so that a minimum number of samples is obtained in each group. The sample in both groups (DM with and without DPN) was 18.

The Diabetic Peripheral Neuropathy group and the group without Diabetic Peripheral Neuropathy are the dependent variables in this study. The independent variable of this study is the thickness of the retinal nerve fiber layer. Retinal Nerve Fiber Layer Thickness was examined using OCT (Cirrus 5000, Carl Zeiss Meditec, Jena, Germany), DPN was diagnosed by neurologist with Electro Neuro Myography (USA Cadwell Sierra Summit ENMG) and DNS-Ina Questioner. The severity of DPN using Consensus Development Conference of Standardized Measured in Diabetic Neuropathy. Ethics of Health Study RSUD Dr. Saiful Anwar Malang Number 400/107/K.3/302/2021 was given.

RESULTS

The DM group with DPN had a greater mean age than the DM group without DPN (54 years and 48 years, respectively). The average HbA1C in DM patients with DPN was 8.47, whereas the average HbA1C in DM patients without DPN was 8.22. Visual acuity was variable in the DM without DPN group, with an average visual acuity of 0.19 logMAR and 0.09 logMAR in the DM with DPN group. DM patients without DPN had an average RNFL of 102.61 micrometers, with 122.22 micrometers in the superior quadrant, 123.50 micrometers in the inferior quadrant, 76.33 micrometers in the temporal quadrant, and 77.39 micrometers in the nasal quadrant. The average RNFL thickness in DM patients with DPN was 100.22 micrometers for each quadrant, particularly the superior quadrant was 125.11 micrometers, the inferior was 128.28 micrometers, the temporal was 71.78 micrometers, and the nasal was 75.11 micrometers.

In the nerve conduction study, the sural nerve amplitude (SNAP) was found to be 17.66 microvolts in the DM group without DPN and 5.72 microvolts in the DM group with DPN. The distal sural latency was found to be 0.87 ms in the non-DPN DM group and 1.37 ms in the DM group with DPN. The sural nerve conduction was found to be 113.72 m/s in the DM group without DPN and 104.72 m/s. The amplitude of the tibial nerve (CMAP) was measured in the DM group without DPN to be 13.07 microvolts and 6.85 microvolts in the DM group with DPN, the distal tibial latency in the DM group without DPN was 4.79 ms and 4.96 ms in the DM group with DPN, while the tibial nerve conduction velocity in the DM group without DPN was 57.22 m/s and 47.11 m/s in the DM group with DPN. Table 1 shows the descriptive data of the respondents.

Table 1. Data distribution

Variable	Group	N	Mean	St dev	95% CI		Minimum	Maximum
					Lower Bound	Upper Bound		
Age	DM non DPN	18	48.89	6.73	45.54	52.24	41	60
	DM DPN	18	54.67	5.89	51.74	57.60	41	60
HbA1c	DM non DPN	18	8.22	1.72	7.36	9.07	6.6	12.3
	DM DPN	18	8.47	1.38	7.79	9.16	6.8	11.6
Duration	DM non DPN	18	3.47	2.12	2.42	4.53	1	7
	DM DPN	18	4.97	2.64	3.66	6.28	0.5	10
Visual Acuity	DM non DPN	18	0.19	0.13	0.14	0.27	0	0.4

RNFL (Average)	DM DPN	18	0.09	0.10	0.04	0.14	0	0.3
	DM non DPN	18	102.61	9.11	98.08	107.14	85	119
RNFL (Superior)	DM DPN	18	100.22	9.38	95.56	104.89	80	110
	DM non DPN	18	122.22	9.61	117.44	127.00	104	141
RNFL (Inferior)	DM DPN	18	125.11	18.00	116.16	134.06	88	153
	DM non DPN	18	123.50	16.25	115.42	131.58	104	156
RNFL (Temporal)	DM DPN	18	128.28	17.57	119.54	137.01	92	156
	DM non DPN	18	76.33	8.53	72.09	80.58	61	99
RNFL (Nasal)	DM DPN	18	71.78	12.21	65.71	77.85	49	94
	DM non DPN	18	77.39	14.00	70.43	84.35	59	118
Sural amplitudo (mikrvolt)	DM DPN	18	75.11	11.38	69.45	80.77	58	97
	DM non DPN	18	17.66	6.47	14.44	20.87	10.90	39.20
Sural distal latency (ms)	DM DPN	18	5.72	3.27	4.09	7.34	0.20	10.90
	DM non DPN	18	0.87	0.76	0.49	1.25	0.10	2.80
Sural conduction velocity (m/s)	DM DPN	18	1.37	1.37	0.68	2.05	0.00	5.30
	DM non DPN	18	113.72	43.83	91.93	135.52	48.00	156.00
Tibia amplitudo (mv)	DM DPN	18	104.72	48.25	80.73	128.72	26.00	156.00
	DM non DPN	18	13.07	3.19	11.48	14.65	7.90	20.20
Tibia distal latency (ms)	DM DPN	18	6.85	4.98	4.37	9.33	0.00	18.60
	DM non DPN	18	4.79	1.99	3.80	5.78	2.50	11.30
Tibia conduction velocity (m/s)	DM DPN	18	4.96	1.73	4.10	5.82	1.30	9.20
	DM non DPN	18	57.22	4.58	54.94	59.50	51.00	66.00
	DM DPN	18	47.11	18.98	37.67	56.55	30.00	106.00

Furthermore, in this study, the gender distribution in the DM group with DPN was 8 males (44.67%) and 10 females (55.56%), whereas the DM group without DPN was 12 males (66.67%) and 6 females (33.33%). With a total of 20 men (55.6%) and 16 women (44.4%). Table 2 shows the results of a thickness assessment using the RNFL and ENMG to estimate the amplitude, latency, and conduction velocity (cv) of both sensory and motor nerves. The normality test results for Age, HbA1c, Duration, and RNFL and ENMG parameters had a p value > 0.05, indicating that the data utilized has a normally distributed distribution, so the correlation test used parametric statistics, specifically the Independent T Test. Whereas the p value for visual acuity variables, distal sural delay, and tibial conduction velocity is 0.05. The comparison test between DM with DPN and DM without DPN employs nonparametric statistics, particularly the Mann Whitney test and Spearman's correlation. Table 3 shows the results of the comparison test for each variable.

Table 2. Respondents Characteristic

Variable	Groups	Characteristic	n	%
Gender	DM non DPN	Female	6	33.33
		Male	12	66.67
	DM DPN	Female	10	55.56
		Male	8	44.44
DNS score	DM non DPN	0	18	100
		1	0	0.00
		2	0	0.00
		3	0	0.00
		4	0	0.00
	DM DPN	0	0	0.00
		1	2	11.11
		2	6	33.33
		3	4	22.22
		4	6	33.33
Severity	DM DPN	Mild	10	55.56
		Moderate	5	27.78
		Severe	3	16.67

Table 3. Comparison Test in Variables

Variable	Groups (Mean±Sd)		p
	DM DPNv(18)	DM non DPNv(18)	
Age	48.88±6.73	54.66±5.89	0.010*
HbA1c	8.22±1.72	8.47±1.38	0.626
Score	0.00±0.00	2.78.0±1.06	0.000 *mw
Duration	3.47±2.12	4.97±2.64	0.068
Visual acuity	0.19±0.13	0.09±.0.1	0.010 *mw
Sural amplitudo (mikrvolt)	17.66±6.47	14.44±20.87	0.000*
Sural distal latency (ms)	0.87±0.76	1.37±1.37	0.187
Sural conduction velocity (m/s)	113.72±43.83	104.72±48.25	0.562
Tibia amplitudo (mv)	13.07±3.19	6.85±4.98	0.000*
Tibia distal latency (ms)	4.79±1.99	4.96±1.73	0.789
Tibia conduction velocity (m/s)	57.22±4.58	47.11±18.98	0.041*

*p<0,05 (statistically significant); mw= mann whitney

There are significant differences in age, DNS score, visual acuity, sural amplitude, tibia amplitude, and tibia conduction velocity, as shown in Table 3.

While the average RNFL, superior RNFL, inferior RNFL, temporal RNFL, and nasal RNFL results in both groups were negligible (p>0.05), they are summarized in Table 4.

Table 4. Comparison test of RNFL

Variables	Groups (Mean±Sd)		p
	DM non DPN (18)	DM DPN (18)	
Average RNFL	102.61±9.11	100.22±9.38	0.444
Superior RNFL	122.22±9.61	125.11±18	0.552
Inferior RNFL	123.50±16.25	128.28±17.57	0.403
Temporal RNFL	76.33±8.53	71.78±12.21	0.203
Nasal RNFL	77.39±14	75.11±11.38	0.596

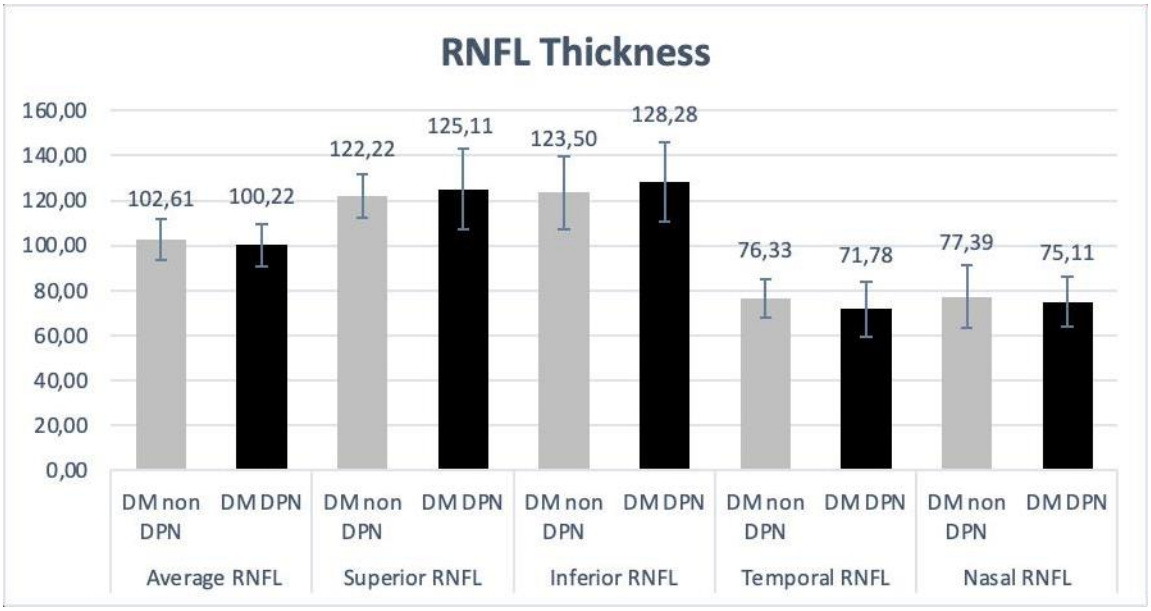

Figure 1. RNFL thickness in DM with and without DPN

Table 5. Correlation between the severity of DPN with RNFL thickness

	r	p
Severity→Average RNFL	-0.285	0.252
Severity→Superior RNFL	0.214	0.394
Severity→Inferior RNFL	0,427	0.077
Severity→Temporal RNFL	-0.258	0.301
Severity→Nasal RNFL	-0.126	0.620

Because the correlation test for all types of RNFL had a p-value more than 0.05, it can be inferred that there was an insignificant relationship between the severity of DPN and the thickness of RNFL. Likewise, age, HbA1C, and duration all exhibited p values more than 0.05, indicating that there was no significant relationship between age, HbA1C, duration, and RNFL thickness.

DISCUSSION

Total of 36 samples were obtained. According to the gender distribution, there were 12 men and 6 women in the DM without DPN group and 8 men and 10 women in the DM with DPN group. Women were shown to have increased neuropathic pain, paresthesias, and loss of sensation in the lower extremities.[6]

There was a disparity in the number of gender comparisons in this study because the samples were taken based on inclusion criteria that excluded the proportion of gender. Gender impacts RNFL thickness, according to study journals, where it is discovered that RNFL thickness in women is thicker than RNFL thickness in males, which is impacted by the hormone estrogen, which has a protective effect on RNFL thickness. Because estrogen administration preserves RGC and RNFL, the neuroprotective effect of estrogen is thought to be mediated via estrogen receptors on Retinal Ganglion Cells (RGC) in animal studies. Postmenopausal women who received estrogen hormone therapy had thicker RNFLs than women who did not get hormone therapy, indicating that estrogen exposure can protect the RNFL and slow the aging process of the optic nerve. [6,7,8] The average age of the women in this study was 50.8 whereas Suryana et al discovered that the average age of menopause for Indonesian women was 50 years, implying that the average sample from this study would enter menopause. [9] The difference in RNFL thickness between men and women can be considered to be 1 micrometer, and some study claim that men have an RNFL thickness of 0.4 micrometers when compared to women.[10] The average RNFL thickness was found to be lower in the DM group with DPN when compared to the DM group without DPN, which is consistent with previous study by Buno et al and Srinivasan et al, which found a concentrated neuropathic effect in the peripapillary nerve fiber layer due to neuronal degeneration that occurs before microvascular abnormalities. [11,12]

According to Altman C and colleagues' study, diabetic retinopathy is a mix of microvascular anomalies and neurodegenerative effects on retinal ganglion cells. According to study, the neurological effects of diabetes may occur before microvascular problems. injury to the blood-retinal barrier and subsequent retinal ganglion injury as a result of edema and elevated extracellular fluid levels. [5,13,14] According to previous study, the neurodegenerative effect of diabetes on ganglion cell and RNFL thickness is primary due to DM and secondary as an aftereffect. Edema and increasing extracellular fluid levels cause damage to the blood retinal barrier and, as a result, to the retinal ganglion.[15] In diabetic neuropathy, metabolic abnormalities and oxidative stress cause the beginning and progression of nerve injury.[16] The polyol pathway's metabolism is the main pathway that connects diabetes mellitus to diabetic peripheral neuropathy; aldose reductase is predominantly found in Schwann cells in peripheral nerves, indicating that the polyol pathway is the main route of diabetic peripheral neuropathy associated with schwannopathy. Furthermore, reactive oxygen species (ROS) created by the cytosol will cause mitochondrial overactivation, which will work in the hexosamine pathway. The dynamics of mitochondrial function alterations may possibly contribute to the neurodegenerative process of diabetic peripheral neuropathy. Nerve conduction investigations often demonstrate a drop in amplitude, increased latency, and a decrease in nerve conduction velocity. Neurodegeneration is thought to occur not just in the peripheral nerves, but also in the central nervous system. There was a substantial difference in lengthening the latency and decreasing the amplitude of N75-P100 on VEP assessment in recent studies. [17,18] We assessed RNFL thickness in diabetes patients and controls, modifying the sample agerange (40-60years) accordingly. The global thickness of RNFL was observed to be lower in the DM group with DPN, which is consistent with earlier study that indicated global RNFL thinning when compared to the DM group with DPN and DM without DPN, albeit this was not statistically significant. In a similar investigation, Sohn EH and colleagues discovered that patients with diabetes but no diabetic retinopathy had thinner RNFL layers than

age-matched controls.[15] The study also found that thinning was observed over four years, and was independent of age, sex, and levels of glycosylated hemoglobin. It can therefore be assumed that retinal nerve degeneration may precede the development of diabetic retinopathy.[19,20] This occurrence differs from a prior study by Bonifacio, who found thinning in the superior, inferior, and overall quadrants in the DM group with DPN but no difference in temporal quadrant RNFL thickness between the two groups. When the RNFL thickness was examined by quadrant, it was discovered that the superior and inferior quadrants of the DM group with DPN had a greater thickness than the superior and inferior quadrant RNFL in the DM group without DPN. Despite the fact that these two parameters are not statistically significant. The difference in the results of this study is that the density of the retinal nerve fibers in each peripapillary area is different, so several previous studies stated that RNFL thinning also occurs in the superior and inferior quadrants and that the inner retinal layer is responsible for the overall retinal thickness. The most likely cause of retinal thickness is damage to the blood-retinal barrier. The RNFL thickness in the peripapillary area changes more than the GCC thickness in the macular area.[21,22]

While the RNFL thickness of the temporal and nasal quadrants of the DM with the DPN group was lower than the RNFL thickness of the temporal and nasal quadrants of the DM without the DPN group, this was not statistically significant. The findings in this study differ from previous studies in that RNFL thickness decreased significantly in the superior and inferior quadrants while there was no difference in temporal RNFL thickness, [23] which may be due to the peripapillary area having higher axon density than the macular area. The progression of the disease in DM patients with DPN varies widely and does not follow a predictable pattern, and the risk of ischemia occurring in the axon is higher, worsening the effects of the neurodegenerative disease.

Because few DM patients with DPN who had undergone cataract surgery and intraocular lens implantation were not excluded from this investigation, the visual acuity in the DM without DPN group in this study was significantly lower than that in the DM group with DPN and the average visual acuity with correction for the DM without DPN group was lower than that of the DM group with DPN because numerous patients in this group started to develop cataracts or lens clouding in the early or immature stages. This is supported by study by Harding et al., which shows that peripheral neuropathy plays a separate role in the development of cataracts. [24]

A significant clinical aspect of DPN is the presence of neuronal atrophy, which happens concurrently with axonal atrophy and causes damage to the axons. This is supported by the concept of neuron- specificity. Functional deficiencies include delayed nerve conduction, decreased amplitude, and extended latency are brought on by the distal axon's atrophy. 25 Uncontrolled hyperglycemia damages nerves by currently unidentified methods, increasing the activity of the polyol pathway by accumulating sorbitol and fructose in them. Along with this, there is a reduction in myo-inositol absorption, inhibition of Na+/K+-adenosine triphosphate with Na+ retention, edema, swelling of the myelin, axoglial disjunction, and nerve degeneration. It has been hypothesized that diabetes may produce diabetic peripheral neuropathy via axonopathy and myelinopathy given the fact that conduction velocity, distal latency, and sural nerve amplitude in diabetic patients all varied considerably by age and gender. Although axonopathy was the primary disease overall and one-third of the nerves displayed demyelination, this finding also reflects

results from clinical and pathological studies where both processes were documented. [26,17]

Children typically have a somewhat larger SNAP amplitude due to their lower skin impedance. Studies on nerve conduction show a little slowdown after the age of 60. A number of morphological and functional aspects of the peripheral nervous system are significantly impacted by aging, including muscle strength, sensory discrimination, autonomic response, and endoneural blood flow. Aging also has an impact on the peripheral nervous system's electrophysiological properties. [27,28] The patients' mean age in this study was 54.66 5.89 years, which suggests that the patient's age had no discernible impact on the SNAP amplitude values we found. [29,30]

Similar results were observed in the nerve conduction velocity of the DPN group, which was discovered to have decreased in comparison to the DM group without DPN. In line with study by Sepat et al., 2020, subjects with diabetes experienced a significant decrease in amplitude and nerve conduction velocity in the sural, median, and also ulnar nerves. The decrease also occurred in the tibial nerve conduction velocity parameter in DM with DPN.Diabetes related nutritional and metabolic alterations that affect axoplasmic transport in peripheral nerves and prevent distal axons from receiving enough nutrition might result in abnormalities of these electrophysiological parameters, which can lead to a process of neurodegeneration. [31,32] Comparing the DNS score distribution between the DM with DPN group and the DM without DPN group, it was discovered that the DM with DPN group had a higher DNS score dispersion. Depending on how severely the peripheral nerve fibers have been damaged, clinical symptoms will vary. [33] The DNS and DNE developed by Meijer were found to be straightforward instruments, simple to use, and quick methods for detecting diabetic neuropathy. The correlation between DNS and nerve conduction studies is significant, according to a study that compared various questionnaires to detect complications of diabetic neuropathy. [34] Therefore, nerve conduction investigations are crucial in the early diagnosis of diabetic neuropathy, and they come to the conclusion that Type 2 Diabetes Mellitus patients have electrophysiological changes indicative of peripheral neuropathy prior to the clinical manifestation of the condition. Doctors can assist prevent long-term problems of diabetes mellitus, such as diabetic ulcers and amputations, by early identifying peripheral neuropathy in Type 2 Diabetes Mellitus patients.

In a recent study, it was discovered that when the diagnosis of DPN is made, there is a multidirectional method that can identify ophthalmological results. According to a number of studies, diabetic peripheral neuropathy affects the thickness of the RNFL, which is made up of the inner neural layer of ganglion cell axons without myelin sheaths. In this study, there was RNFL, temporal, and nasal quadrant global/average thinning. Although this difference was not statistically significant overall, thicker RNFL was seen in the superior and inferior quadrants in the DM group with DPN. In contrast to the study presented by Fawzy et al, where the superior quadrant is thinner than the other quadrants, this one does not.[35] In this study, it was discovered that the HbA1c level had no discernible impact on RNFL thickness in either the DM group with DPN or the DM group without DPN. A similar study, proposed by Srinivasan et al., also produced results that were broadly consistent with these findings.[11] The distribution of Diabetic Peripheral Neuropathy severity in this study was imbalanced, with 3 DPN patients

having severe severity, 5 having moderate severity, and 10 having mild severity. The results of this study are in contrast to those of a study done in 2019 by Nurlaela et al, which found that most DPN damage at Dr. Saiful Anwar Hospital is severe severity. This is because patients with severe DPN have typically encountered macrovascular or other microvascular problems. such as Diabetic Retinopathy, Kidney Failure, Coronary Heart Disease, Stroke, and others that will not be included in this study. [36] Early diabetes that has not yet developed as diabetic retinopathy will see an increase in RNFL thickness volume first due to the rise in RNFL thickness on the superior and inferior. This is supported by the theory of activation of microglia cells like Muller cells, where Diabetes induces hypertrophy and activation of Muller cells which will increase the secretion of cytokines and pro-inflammatory molecules from damaged cells to start the regeneration process, manifesting as thickening of the RNFL in the initial phase and in the process axonal degeneration then the thickness of the RNFL will thin due to dysfunction of nerve fiber regeneration. [37] In order to demonstrate clinically that neurodegenerative changes in the peripheral nerves are followed by structural changes of the RNFL, this study compares the thickness of the RNFL between groups of diabetic patients with DPN and DM patients without DPN before the development of diabetic retinopathy. It also examines the relationship between the severity of DPN and RNFL thickness, which has not been done in prior studies. Unfortunately unproportional amount of samples in T2DM with DPN Group 2 was limitation on this study.

CONCLUSION

We observed Retinal Nerve Fiber Layer thinning at average, temporal, and nasal in T2DM with DPN compared to T2DM without DPN. There is a negative correlation between the severity of DPN and Retinal Nerve Fiber Layer Thickness, this indicates the progression of the disease in DM patients with DPN varies widely and does not follow a predictable pattern, and the risk of ischemia occurring in the axon is higher, worsening the effects of the neurodegenerative disease. Further research with a proportional amount of sample in each severity group is needed to get statistically signification correlative results, Regular follow-up to measure the retinal nerve fiber layer thickness is needed to look for progressivity thinning of RNFL and stronger correlation. Thinning of RNFL in T2DM with DPN is an early change of anatomical structure in OCT examination. This newness hopefully increases the awareness of diabetic retinopathy complications. Multidisciplinary management, regular checks up, and comprehensive therapy is recommended to minimize further damage to Diabetes Mellitus.

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