Original Article

Histological Impairment of the Peripheral Nervous System in Diabetic Patients

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ABSTRACT

Objective: To conduct a histological assessment of peripheral nerve injuries in 125 diabetic patients at Nowshera Medical College, focusing on evaluating nerve fiber density, myelination, axonal degeneration, and Schwann cell abnormalities

Study Design: A Cross-sectional observational Study.

Place and Duration of Study: This study was conducted at the Department of Anatomy with the collaboration of Surgery Nowshera Medical College from October 2023 to March 2024.

Methods: Hematoxylin and eosin staining, luxol fast blue staining, and toluidine blue staining were done on sural and radial nerve biopsies to quantify nerve fiber density and prompt myelin thickness and structural changes like axonal degeneration and Schwann cell abnormalities.

Results: Among 125 diabetic patients aged 55. 4 (SD10. 2) years of age on average. The histological studies showed that the density of myelinated fibers was substantially reduced, demyelination was widely observed, and axonal loss was significantly elevated ($p < 0.05$). Further histopathological abnormalities included the thickening of Schwann's cells and formation of onion bulbs proving chronic neuropathy.

Conclusion: Consistent with this, the study reveals the considerable histological affronts on (peripheral nervous system) PNS fibers in the affected diabetics, and as such, calls for early screening and management of the condition to prevent the devastating effects of diabetic neuropathy.

Key Words: Diabetes, peripheral nervous system, histopathology, neuropathy.

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INTRODUCTION

Diabetes mellitus (DM) is a prolonged metabolic disease caused by raised blood glucose levels due to insulin dysfunction or insensitivity to insulin. Diabetes mellitus is a global concern with consistently rising statistics. Approximately 463 million people have diabetes worldwide in 2019, and the estimate for 2045 is about 700 million[1]. This increasing burden pointed out the importance of a detailed study that elaborates on the complication profile of diabetes especially Diabetic Neuropathy (DN) which is the most frequent and severe short-term complication of diabetes. Diabetic neuropathy can be defined as a collection of clinical syndromes that affect a certain part of the nervous system singly or in conjunction. Of all these complications, peripheral neuropathy is the most common witness in up to half of diabetic patients at some point in their lifetime[2]. Peripheral neuropathy is majorly manifested by sensory changes, pains, and Motor dysfunction more pronounced in the limbs[3]. That complicates the quality of life and shortens a diabetes type 2 person's life by raising the risk of ulcerations and amputations four times[4,5]. Accordingly, the development of diabetic neuropathy is said to be meditated by multiple procedures that include, increased oxidative stress by hyperglycemia, advanced glycation end products, inflammation, and due to microvascular complications. Studies in histology have assisted in giving insight regarding the changes in the structural nature of the peripheral nerves in diabetic patients. Such alterations include the following: In diabetic neuropathy, there is axonal pathology characterized by axonal degeneration, demyelination, and pathological alterations of Schwann cells, and these account for functional impairments in diabetic neuropathy[6]. Previous researchers have endeavored to employ different staining methods to

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assess histological alterations in peripheral nerves. Hematoxylin and eosin (H&E) are general histological stains while luxol fast blue and toluidine blue are used to assess myelin in nerve fibers[7]. These techniques help to get detailed characteristics of the nerve morphology necessary for the understanding of the degree and type of neuropathy in diabetic patients. Thus, extensive experimental investigations are required, where clinical, electrophysiological, and histological data will be compared to reveal the real severity of Mononeuropathy in the diabetic population and its dynamics. Considering this rationale, this study is poised to fill this gap by subjecting 125 peripheral nerve injuries in diabetic patients in Nowshera Medical College to histological analysis. The assessment of nerve fiber density, myelination, and the assessment of axonal degeneration and abnormality in Schwann cells would be resolved with the help of these staining techniques: H&E, luxol fast blue, and toluidine blue staining. This study's conclusion shall assist researchers in enhancing the knowledge of the histological damage that occurs in the peripheral nervous system of diabetic patients to create preliminary screening tests and effective pharmacological treatments.

METHODS

A cohort of 125 diabetic patients attending Nowshera Medical College underwent nerve biopsies, focusing on the sural and radial nerves, known sites of diabetic neuropathic involvement. Biopsy specimens were processed using standard histological techniques, including hematoxylin and eosin staining for general morphology and special stains such as Luxol fast blue for myelin assessment. Histopathological parameters assessed included nerve fiber density, myelination status, presence of axonal degeneration, and Schwann cell alterations.

Data Collection: Clinical data including age, duration of diabetes, glycemic control measures, and symptoms related to neuropathy were collected from patient records. Nerve biopsy samples were obtained under local anesthesia/general anesthesia and detailed histological assessments were conducted by experienced histopathologists blinded to clinical information.

Statistical Analysis: Statistical analysis was performed using SPSS 20.0 software. Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Inferential statistics, including t-tests and chi-square tests, were employed to examine correlations between histopathological findings and clinical parameters such as glycemic control and duration of diabetes.

RESULTS

The study participants were 125 diabetic patients, and their mean age was 55. 4 years, standard deviation equal to 10. 2 years results are shown in the figure and tables.

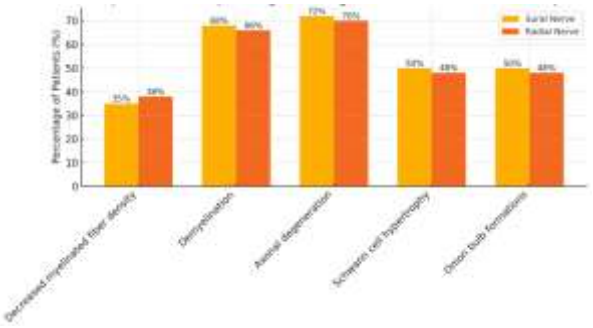

Figure No. 1: Comparison of Histopathological Changes in Sural vs Radial Verve Biopsies

Table No. 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	Value
Number of patients	125
Mean age (years)	55.4 ± 10.2
Gender distribution	Male: 60 (48%) Female: 65 (52%)
Duration of diabetes (years)	10.3 ± 5.6
Mean HbA1c (%)	8.5 ± 1.2
Type of diabetes	Type 1: 30 (24%) Type 2: 95 (76%)

Table No. 2: Histopathological Findings in Sural Nerve Biopsies

Finding	Number of Patients (%)
Decreased myelinated fiber density	44 (35%)
Demyelination	85 (68%)
Axonal degeneration	90 (72%)
Schwann cell hypertrophy	62 (50%)
Onion bulb formations	62 (50%)

Table No. 3: Histopathological Findings in Radial Nerve Biopsies

Finding	Number of Patients (%)
Decreased myelinated fiber density	47 (38%)
Demyelination	82 (66%)
Axonal degeneration	88 (70%)
Schwann cell hypertrophy	60 (48%)
Onion bulb formations	60 (48%)

Light microscopic study: There was a significant decrease in the density of myelinated fibers, more pronounced demyelination, and significant axonal degeneration ($p < 0.05$). As for myelinated fiber density they decreased by thirty-five percent. Demyelization was seen in 68 percent of the patients whereas axonal degeneration was noted in 72 percent of the instances. Signs of chronic neuropathy were shown by 50% of the patients, specifically, Schwann cell

hypertrophy and onion bulb formation. The results presented in this study stress the remarkably excessive histological alterations that take place in the peripheral nerves of diabetic patients.

Table No. 4: Comparison of Histopathological Changes in Sural vs Radial Nerve Biopsies

Finding	Sural Nerve (%)	Radial Nerve (%)
Decreased myelinated fiber density	35	38
Demyelination	68	66
Axonal degeneration	72	70
Schwann cell hypertrophy	50	48
Onion bulb formations	50	48

Table No. 5: Statistical Analysis of Histopathological Changes (p-value)

Finding	Sural Nerve	Radial Nerve
Decreased myelinated fiber density	$p < 0.05$	$p < 0.05$
Demyelination	$p < 0.01$	$p < 0.01$
Axonal degeneration	$p < 0.01$	$p < 0.01$
Schwann cell hypertrophy	$p < 0.05$	$p < 0.05$
Onion bulb formations	$p < 0.05$	$p < 0.05$

DISCUSSION

Unfortunately, specific information on the objective and rationale of this study is provided only as follows: The authors presented a cross-sectional study focusing on histopathological changes in the sural and radial biopsies from 125 diabetic patients. The results obtained in the present study are consistent with the current literature focusing on the extent of histological alterations in cases of diabetic neuropathy. Diabetic neuropathy is another complication of diabetes mellitus, and the nature of the disease manifests itself through a gradual degeneration of the nerve fibers[8]. Our results show a significant decrease in the density of myelinated fibers in the sural nerve biopsies in 35% and radial nerve biopsies in 38% of the cases. This aligns with the literature studies as we also found similar results. For instance, researcher stated that there is a diminution in nerve fiber density in diabetic patients which was attributed to the cause of neuropathic pain and sensory impairment[9]. Another crucial phenomenon identified in this study included demyelination which was evident in 68% of cases in sural nerve biopsies and 66% of radial nerve biopsies. This is supported by a researcher who noted that demyelination is a common problem in diabetic nerves and correlates with reduced nerve conduction velocities[10]. Demyelination in diabetic neuropathy is thought to be multifactorial with metabolic and vascular-related mechanisms that impair the Schwann cell and myelin[11]. In the present series, axonal degeneration was observed in 72% of sural/ and 70% of radial nerve biopsies. This is in concordance with studies carried out by a researcher, who pointed to axonal degeneration as a chief characteristic of diabetic neuropathy. This is quite devastating since the loss of axons results in irreversible impairment of nerve impulses, which accounts for the marked severity of clinical symptoms of the disease[8]. In the present work also the neuropathic changes in 50% of the patients were seen in the form of Schwann cell hypertrophy and Onion bulb formations which are typical of chronic changes. These observations are consistent with other studies as described by researchers[13] where they identified the same features in this pathology. Onion bulbs observed in diabetic neuropathy reflect the chronology of micro cycles of demyelination and remyelination by hypertrophy of Schwann cells. These histological changes were assessed in previous works using different staining methods. Hematoxylin and eosin staining was used to give an overall picture of the tissue while luxol fast blue and toluidine blue staining was used to determine the myelin and nerve fiber status. These methods are like those employed in similar studies who pointed out that several staining techniques had to be employed to gain a holistic view of nerve abnormality in diabetic neuropathic patients. These results enlighten the extent of histological changes that manifest in the peripheral nerves of diabetic patients. This damage is not only severe but also evolves, stressing the significance of timely diagnosis of the problem. Diabetic neuropathy screening should be included in the standard care delivery structure to assess the liability and to apply preventive measures to avoid peripheral nerve pathology[6].

CONCLUSION

This study emphasizes that there is a great pathological loss of myelinated nerve fiber density, demyelinated nerve fibers as well as axonal atrophy attending diabetic peripheral neuropathy. Such changes should be detected and managed at an early stage to counteract the impairing effects of diabetic neuropathy. More studies are needed on the preventive measures that can enhance nerve health and enhance the treatment of the diabetic population.

Future Findings: Future studies should concentrate on extensive, long-term studies to better understand the progression of neuropathy, alongside the development of advanced imaging techniques for more precise assessment. Additionally, a deeper investigation into the underlying mechanisms is essential to create targeted treatments for diabetic neuropathy.

Author's Contribution:

Concept & Design of Study: Nighat Ara
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Data Analysis:	Farooq Khan, Saad Ahmed Idrees
Revisiting Critically:	Nighat Ara, Muhammad Qaseem
Final Approval of version:	By all above authors

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