Original Article

Prevalence of Peripheral Neuropathy in Pediatric Patients with Type 1 Diabetes Mellitus

Nazir Ahmed Malik[1], Nimra Naheed Malik[2], Somayia Sidiqa[1], Somayia Javed[3] and Tabassum Fatma[4]

ABSTRACT

Objective: The objective of this study was to study the prevalence of peripheral neuropathy in pediatric patients suffering from type 1 diabetes mellitus.

Study Design: A multicenter cross-sectional study.

Place and Duration of Study: This study was conducted at the HITEC-IMS Taxilla, Al -Ihsan Hospital Rawalpindi & Nusrat Hospital Rawalpindi from Jan 2023 to August 2023.

Methods: The study invited parents of paediatrics patients with type 1 diabetes to participate. Participating parents who consented were provided with questionnaires, encompassing neurological examinations and assessments of nerve dysfunction through nerve conduction studies (NCS). The questionnaire also gathered comprehensive information on demographics, family status, education level, chronic illnesses, weight, height, BMI, and access to the healthcare system. NCS procedures were meticulously explained to the participants and conducted using the standard "Alleger's Scorpio Electromyography machine" in a room maintained at an optimal temperature of 72 degrees Fahrenheit. Skin temperature, recorded at 97 degrees Fahrenheit, and ideal lighting conditions were ensured during the examination. The selected nerves for the procedure included median, ulnar, tibial, peroneal, and sural nerves. Reference values for NCS were obtained from a clinician specializing in neuromuscular disorders in infancy, childhood, and adolescence. With parental permission, blood samples were collected to measure blood glucose, HbA1c, Liver Function Tests (LFTs), vitamin B12, lipid profile, thyroid-stimulating hormone (TSH), urea, and creatinine in the children.

Results: The findings from this research indicate that prevalence of peripheral neuropathy in children with type 1 diabetes is 46%. There is a noteworthy association between glycemic control and the prevalence of peripheral neuropathy. The study's overall outcome reveals a 55.2% increase in nerve conduction per unit of HbA1C. The mean age of the study population is 12.8±3.665 years. Notably, the results of nerve conduction studies (NCS) are statistically significant. Furthermore, there are no significant differences observed between the groups concerning lipid profile, vitamin B12 levels, thyroid-stimulating hormone (TSH), urea, and creatinine.

Conclusion: The prevalence of diabetic neuropathy in children is 46%. Major risk factors in this condition are the duration of the disease and uncontrolled glucose level. The use of nerve conduction studies is more reliable than clinical evaluation for the diagnosis of neuropathy. Moreover, neuropathy has a direct relation with elevated levels of glucose. There is no evidence of retinopathy.

Key Words: diabetes, nerve conducting studies, juvenile diabetes, glucose level.

Citation of article: Malik NA, Malik NN, Sidiqa S, Javed S, Fatma T. Prevalence of Peripheral Neuropathy in Pediatric Patients with Type 1 Diabetes Mellitus.Med Forum 2024;35(3):8-12.doi:10.60110/medforum.350302.

INTRODUCTION

[1.] HIT Hospital Taxila, Rawalpindi.
[2.] Al Ehsan Hospital Rawalpindi
[3.] Nusrat Hospital Rawalpindi
[4.] Shifa Trust Eye Hospital, Rawalpindi

Correspondence: Dr. Nazir Ahmed Malik, Child Specialist, HIT Hospital Taxila, Rawalpindi.
Contact No: 03337613234
Email: drnamalik@hotmail.com

Received: November, 2023
Accepted: January, 2024
Printed: March, 2024

Diabetes Mellitus (DM) is a metabolic disease characterized by elevated blood glucose levels[1]. It constitutes a significant global health issue. The global estimate indicates that in 2021, approximately 8.4 million people had T1DM worldwide and by 2040, the number of people living with T1DM is projected to reach 17.4[1].

Diabetes is mainly caused by elevated levels of glucose for longer periods. Diabetes may result from either a deficiency in insulin secretion, a reduction in insulin effectiveness, or a combination of both factors[2].Type 1 diabetes, also known as juvenile diabetes or Insulin-dependent diabetes, typically results from the destruction of beta cells, leading to a deficiency in insulin[3]. Diabetes, if undiagnosed for a long period can lead to other major problems like cardiovascular

disease, kidney malfunction, retinopathy, neuropathy, and foot amputation[4].

Neuropathy, a significant complication of diabetes, manifests in both type 1 and type 2 diabetes, impacting 60% of the population in the Western world[5]. Retinopathy and nephritis have also been seen in young populations suffering from type 1 diabetes[6]. 10% of children have complained about peripheral neuropathy with type 1 diabetes which includes the signs and symptoms in the lower limbs[7].

Along with the peripheral nervous system, diabetes can also affect the autonomic nervous system. Peripheral neuropathy caused by diabetes mellitus is usually referred to as polyneuropathy[8]. The effect of diabetes on the nervous system can be divided into 2 stages which are subclinical and clinical. Subclinical refers to electrophysiological abnormalities in nerve function without evident clinical signs or symptoms of peripheral neuropathy. In contrast, clinical neuropathy implies an abnormal neurological examination that shows evident impairment in peripheral sensory and motor polyneuropathy[9,10]. Metabolic theory suggests that when the levels of glucose are elevated they damage nerve cells which leads to the accumulation of sorbitol and because of that myoinositol levels drop hence resulting in damage to nerve and myelin[11].

The diagnosis of diabetic peripheral neuropathy is based upon symptom profile, neurological examination, quantitative sensory testing, nerve conduction studies (NCS), and quantitative autonomic function testing[12]. Neuropathy due to other causes such as Charcot Marie Tooth Disease and Guillain-Barre syndrome should be ruled out while diagnosing diabetic neuropathy[13].

Different nerve fibers including motor, sensory and autonomic must be assessed thoroughly to confirm the origin of disease. Sensory neuropathy is the most common peripheral neuropathy. There are certain non-neuropathic conditions that resemble peripheral neuropathy that should be ruled out in individuals with a lack of sensory involvement. Autonomic dysfunction can occur with all kinds of neuropathies. Wasting of muscles and fatigue is more common in foot extensor muscles which may lead to foot drop[14].

Electromyography and nerve conduction studies should be done to rule out the clinical diagnosis of peripheral neuropathy. Laboratory assessment includes an initial metabolic profile comprising of blood glucose levels, HbA1C, liver, kidney and thyroid functions. Additionally, medical professionals typically order tests based on a thorough clinical evaluation to help guide diagnosis and treatment[15]. Other tests include examination of cerebrospinal fluid, genetic testing, nerve biopsy, peripheral nerve imaging which is done with nerve ultrasound or MRI[16].

METHODS

This cross-sectional multicentre study was conducted in HIT hospital Taxilla, Rawalpindi, Al-Ihsan Hospital Rawalpindi & Nusrat Hospital Rawalpindi. The duration of study was from January 2023 to August 2023. The study invited parents of paediatrics patients with type 1 diabetes to participate. The objective was to ascertain the prevalence of peripheral neuropathy in this specific demographic region. Participating parents who consented were provided with questionnaires, encompassing neurological examinations and assessments of nerve dysfunction through nerve conduction studies (NCS). The questionnaire also gathered comprehensive information on demographics, family status, education level, chronic illnesses, weight, height, BMI, and access to the healthcare system. NCS procedures were meticulously explained to the participants and conducted using the standard "Alleger's Scorpio Electromyography machine" in a room maintained at an optimal temperature of 72 degrees Fahrenheit. Skin temperature, recorded at 97 degrees Fahrenheit, and ideal lighting conditions were ensured during the examination. The selected nerves for the procedure included median, ulnar, tibial, peroneal, and sural nerves. Reference values for NCS were obtained from a clinician specializing in neuromuscular disorders in infancy, childhood, and adolescence. With parental permission, blood samples were collected to measure blood glucose, HbA1c, Liver Function Tests (LFTs), vitamin B12, lipid profile, thyroid-stimulating hormone (TSH), urea, and creatinine in the children.

Statistical Analysis:

The data was summarized for quantitative analysis based on demographic traits, height, weight, and nerve conducting studies. The mean and standard deviation were calculated for each continuous data parameter to derive average results. Parametric tests, including one-way analysis of variance (ANOVA), student's t-test, and chi-square, were employed to compare the groups. Shapiro-Wilk test is used to assess the normality of data. SPSS Version 23 was used for statistical analysis of data by setting the level of significance to less than 0.05 p value. Mainly the study's focus is to provide the awareness on prevalence of peripheral neuropathy in children and adolescents.

RESULTS

There were 100 participants in the study. 45 patients were males and 55 were females. There were 30 children with age 4 to 7 and 70 with 10-14 years. There were no children with chronic illness other than diabetes. The mean age of the study population is 12.8±3.665. There was no sign of retinopathy. The prevalence of peripheral neuropathy was 46%. A high amount of prevalence was seen in children of age 4-14. The result of NCS was significant. The prevalence of peripheral neuropathy with glycemic control is significant. The overall result of the study shows that nerve conduction increases by 55.2% as per unit of HbA1C.

Table No. 1: Demographic Characteristics

Demographics		Frequency	Percentage
Gender	Male	45	45%
	Female	55	55%
Age in years	4-7	30	30%
	10-14	70	70%
Chronic disease other than diabetes	yes	0	0%
	no	100	100%

Table No. 2: Mean and SD for age,duration of disease, HbA1C (n=100)

Parameter	Mean	SD
Age in years	12.8	3.665
Duration of disease in years	6.8	2.148
HbA1C	10.9	1.82

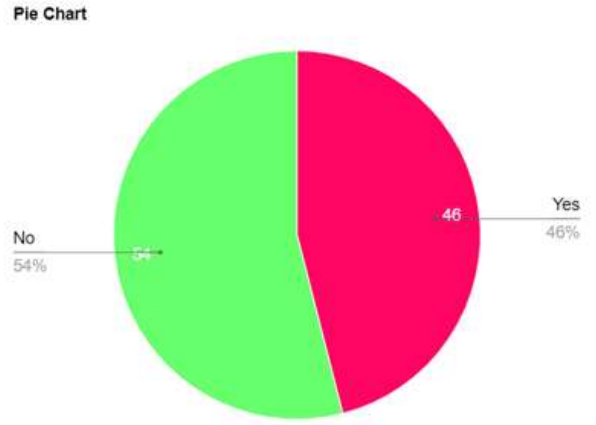

Figure No. 1: Prevalence of peripheral neuropathy

Table No. 3: Comparison of NCS & HbA1C in patients with and without neuropathy

	Mean	SD	P value
NCS			
Normal	5.0	1.442	0.05
Neuropathic	5.8	2.704	
Mean HbA1c level			
No neuropathy	10.6	1.674	<0.001
Neuropathy	11.2	1.799	

Table No. 3: Comparison of glycemic control with prevalence of neuropathy

Neuropathy	Good control (<=8.5)	Fair control (6.6-7.6)	Poor control (>9)
No	1%	76.9%	40%
Yes	0	23.1%	60%

DISCUSSION

The purpose of this study is to know the prevalence of neuropathy in children with Type 1 diabetes mellitus. A total of 100 children were assessed with type 1 diabetes, who had this disease since last five years.

This study shows that type 1 diabetes is more common in females as compared to males. Our study results are comparable with another study conducted in India[4].

A significant number of children with Type 1 Diabetes Mellitus may have subclinical peripheral neuropathy, meaning nerve dysfunction that is not clinically evident. Poor glycemic control and a longer duration of diabetes are mentioned as risk factors for the development of nerve dysfunction in these children[17].

The Rochester Diabetic Neuropathy Study focused on individuals with Type 1 Diabetes Mellitus (T1DM) who had diabetic neuropathy. The study revealed that among these patients, 54% exhibited polyneuropathy, indicating nerve damage affecting multiple peripheral nerves. Additionally, 22% presented with asymptomatic carpal tunnel syndrome, a condition involving pressure on the median nerve in the wrist, and 11% had symptomatic carpal tunnel syndrome.

Furthermore, 7% of the T1DM patients in the study showed signs of visceral autonomic neuropathy, which affects the nerves regulating internal organs. Lastly, 3% displayed other types of neurological damage, suggesting a diverse range of neuropathic complications in this population[18].

According to our study the mean duration of disease is 6.8±2.148. Comparable results were quoted in a meta-analysis done in Pakistan on adult diabetic patients[19]. Toopcizadeh et al ,in their study found that there was no statistically significant difference between age, chronicity of disease and glycemic control between the groups of patients with and without peripheral neuropathy[20].

Our study results of the relation between neuropathy and HbA1c are same as in the previous studies which is significantly correlated i-e "p"<0.001[17,21]. Ziegler et al quoted in his study that neuropathy can be prevented by achieving a good glycemic control in the initial years after developing the disease[22]. However there are studies which show that there is no correlation between neuropathy and HbA1C[23,24]. The nerve conduction increases by 55.2% for every unit increase in HbA1C. This can be compared with other studies 5.2%[17], 27.5%[19] and 13.2%[3] in regards to peripheral neuropathy.

This study has reviewed the glucose and HbA1c levels in the blood and their effects on peripheral neuropathy. However, its impact on brain and spinal cord in the individuals suffering from peripheral neuropathy is beyond the scope of discussion. There was no evidence of retinopathy on evaluation. The BMI and lipid profile of all the children were normal.

More accurate results can be seen in studies performed for longer duration. We could not assess other factors of neuropathy in diabetes mellitus due to economic constraints.

CONCLUSION

The prevalence of diabetes neuropathy in children with type 1 diabetes is 46%. Major risk factors in this condition are the duration of the disease and uncontrolled glucose level. The use of nerve conduction studies is more reliable than clinical evaluation for the diagnosis of neuropathy. Moreover, neuropathy has a direct relation with an elevated level of glucose. There is no evidence of retinopathy.

Author's Contribution:

Concept & Design of Study:	Nazir Ahmed Malik
Drafting:	Nimra Naheed Malik, Somayia Sidiqa
Data Analysis:	Somayia Javed, Tabassum Fatma
Revisiting Critically:	Nazir Ahmed Malik, Nimra Naheed Malik
Final Approval of version:	Nazir Ahmed Malik

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None
Ethical Approval: No.AJK-AP/85 Dated 01.12.20222

REFERENCES

1. Mahase E. Type 1 diabetes: Global prevalence is set to double by 2040, study estimates. BMJ 2022 [cited 2023 Dec 16];378:o2289.
2. Petersmann A, Nauck M, Müller-Wieland D, Kerner W, Müller UA, Landgraf R, et al. Definition, classification and diagnostics of diabetes mellitus. J Lab Med 2018;42(3):73-9.
3. Walter-Höliner I, Barbarini DS, Lütschg J, Blassnig-Ezeh A, Zanier U, Saely CH, et al. High prevalence and incidence of diabetic peripheral neuropathy in children and adolescents with type 1 diabetes mellitus: results from a five-year prospective cohort study. Pediatr Neurol 2018;80:51-60.
4. Daasara G, Gowda VK, Nanjundappa N, Nagarajappa VH, Shivappa SK. Prevalence of Peripheral Neuropathy in Children with Type 1 Diabetes Mellitus. 2022.
5. Kakizawa H, Itoh M, Itoh Y, Imamura S, Ishiwata Y, Matsumoto T, et al. The relationship between glycemic control and plasma vascular endothelial growth factor and endothelin-1 concentration in diabetic patients. Metabolism 2004;53(5):550-5.
6. Cai F, Helke CJ. Abnormal PI3 kinase/Akt signal pathway in vagal afferent neurons and vagus nerve of streptozotocin-diabetic rats. Molecular Brain Res 2003;110(2):234-44.
7. Papanas N, Maltezos E. The diabetic hand: a forgotten complication? J Diabetes and its Complications 2010;24(3):154-62.
8. Olsen BS, Sjølie A-K, Hougaard P, Johannesen J, Borch-Johnsen K, Marinelli K, et al. A 6-year nationwide cohort study of glycaemic control in young people with type 1 diabetes: risk markers for the development of retinopathy, nephropathy and neuropathy. J Diabetes Complications 2000;14(6):295-300.
9. Weintrob N, Amitay I, Lilos P, Shalitin S, Lazar L, Josefsberg Z. Bedside neuropathy disability score compared to quantitative sensory testing for measurement of diabetic neuropathy in children, adolescents, and young adults with type 1 diabetes. J Diabetes Complications 2007;21(1):13-9.
10. Karsidag S, Moralı S, Sargın M, Salman S, Karsidag K, Us O. The electrophysiological findings of subclinical neuropathy in patients with recently diagnosed type 1 diabetes mellitus. Diabetes Res Clin Practice 2005;67(3):211-9.
11. Carrazana E, Mikoshiba I. Rationale and evidence for the use of oxcarbazepine in neuropathic pain. J Pain Symptom Management 2003;25(5):S31-S5.
12. Charles M Soedamah-Muthu SS, Tesfaye S, Fuller JH, Arezzo JC, Chaturvedi N, et al. Low peripheral nerve conduction velocities and amplitudes are strongly related to diabetic microvascular complications in type 1 diabetes: the EURODIAB Prospective Complications Study. Diabetes Care 2010;33(12):2648-53.
13. Overell JR. Peripheral neuropathy: pattern recognition for the pragmatist. Postgraduate Med J 2012;88(1036):88-96.
14. Lehmann HC, Burke D, Kuwabara S. Chronic inflammatory demyelinating polyneuropathy: update on diagnosis, immunopathogenesis and treatment. J Neurol Neurosurg Psychiatr 2019;90(9):981-7.
15. Lehmann HC, Wunderlich G, Fink GR, Sommer C. Diagnosis of peripheral neuropathy. Neurological Res Practice 2020;2:1-7.
16. Telleman JA, Grimm A, Goedee S, Visser LH, Zaidman CM. Nerve ultrasound in polyneuropathies. Muscle Nerve 2018;57(5):716-28.
17. Daasara G, Gowda VK, Nanjundappa N, Nagarajappa VH, Shivappa SK. Prevalence of Peripheral Neuropathy in Children with Type 1 Diabetes Mellitus. DOI: 10.1007/s12098-021-03742-4.
18. Louraki M, Karayianni C, Kanaka-Gantenbein C, Katsalouli M, Karavanaki K. Peripheral neuropathy in children with type 1 diabetes. Diabetes Metabolism 2012;38(4):281-9.
19. Akhtar S, Hassan F, Saqlain SR, et al. The prevalence of peripheral neuropathy among the patients with diabetes in Pakistan: a systematic review and meta-analysis. Sci Rep 2023;13:11744. https://doi.org/10.1038/s41598-023-39037-1

20. Toopchizadeh V, Shiva S, Khiabani N-Y, Ghergherechi R. Electrophysiologic pattern and prevalence of subclinical peripheral neuropathy in children and adolescents with type I diabetes mellitus in Iran. Saudi Med J 2016;37(3):299.
21. Lee SS, Han HS, Kim H. A 5-yr follow-up nerve conduction study for the detection of subclinical diabetic neuropathy in children with newly diagnosed insulin-dependent diabetes mellitus. Pediatr Diabetes 2010;11(8):521-8.
22. Ziegler D, Behler M, Schroers-Teuber M, Roden M. Near-normoglycaemia and development of neuropathy: a 24-year prospective study from diagnosis of type 1 diabetes. BMJ Open 2015;5(6):e006559.
23. Höliner I, Haslinger V, Lütschg J, Müller G, Barbarini DS, Fussenegger J, et al. Validity of the neurological examination in diagnosing diabetic peripheral neuropathy. Pediatr Neurol 2013;49(3):171-7.
24. Coutinho dos Santos LH, Bruck I, Antoniuk SA, Sandrini R. Evaluation of sensorimotor polyneuropathy in children and adolescents with type I diabetes: associations with microalbuminuria and retinopathy. Pediatr Diabetes 2002;3(2): 101-8.