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Prevalence of Peripheral Neuropathy and its Related Factors in Diabetic Children, Neishabour City, Iran

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Abstract

Background

One of the most common metabolic diseases is diabetes mellitus (DM), which its prevalence is growing trend. Early diagnose peripheral neuropathy (DPN) in early stages of patients with DM contributes to metabolic control and prevents severe complications. We aimed to determine the prevalence of peripheral neuropathy (PN) and its related factor in Diabetic children.

Materials and Methods

This cross-sectional study was performed among 60 children with diabetes (type 1) who referring the pediatric endocrinology clinic of Hakim Hospital, Neyshabur city, Iran, in 2016. The neurological symptom score was used for the assessment of neurological features. Neuropathy disability score (NDS) was obtained from the examination of vibration perception (by means of a 128-Hz tuning fork). Peripheral vascular examination was also carried out via evaluating dorsalis pedis and posterior tibial pulses by a neurologist.

Results

The mean age of the children was 10.8±3.38 years. About 56.2% of the patients were female. Diabetic peripheral neuropathy (DPN) score was moderate in 6.7% of the children and it was mild in 38.3% of them. In general, 23% of the children with hemoglobin A1C (HbA1c) higher than the normal range had PN. Assessment of the degree of DPN based on duration of diabetes showed a significant difference among the participants (P=0.05). The study of HbA_{1C} rate based on different degrees of DPN showed a significant difference (P=0.001). In addition, we found a significant difference in FBS score between the children with DPN and children without it (P=0.01).

Conclusion

According the results, more than 23% of children with diabetes had DPN, and the duration of diabetes was a related factor in PN. Therefore, neurological assessment including nerve conduction studies and meticulous physical examination should be performed for evaluating the function of large sensory and motor fibers.

Key Words: Children, Diabetes Mellitus, Hemoglobin A1C, Peripheral Nervous System Diseases.

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1- INTRODUCTION

Diabetes mellitus (DM) is known as the most common metabolic disease, in which the ability of the body to take energy from food is impaired (1, 2). The prevalence of this disease is on a growing trend; based on the World Health Statistics 2016, about 422 million adults are suffering from diabetes mellitus (3). The global prevalence of this problem among adults has increased from 4.7% in 1980 to 8.5% in 2014 (4). In 2001, the prevalence of diabetes among children was 1.48 per 1000 cases, which increased to 1.93 in 2009 (5). Type 1 and type 2 diabetes, diabetes due to genetic defects of β-cell function, and gestational diabetes are the four major types of diabetes. Frequent urination and increased thirst and hunger are the common symptoms of diabetes (1).

Type 1 diabetes, which results from a T cell-mediated beta cell destruction of the pancreas and leads to absolute insulin deficiency, constitutes 5–10% of patients with diabetes. Type 2 diabetes is referred to as non–insulin-dependent diabetes and observed in about 90–95% of diabetic patients. There is broad agreement that diabetes prevention is critically important; however, there is still controversy over the particular intervention for this purpose (6). The effectiveness of lifestyle changes for diabetes prevention has been shown in several studies (7-9). Nonetheless, patients can hardly adapt themselves with the new lifestyle (10). In the absence of treatment, diabetes can cause many complications. Diabetic patients experience serious long-term complications including neuropathy, retinopathy, nephropathy, and macrovascular disease (11). Diabetic neuropathy (DN) is a major cause of morbidity and poor quality of life in patients with diabetes mellitus. It can increase the chances of other complications, namely amputation and foot ulcer (12). The prevalence of DN is estimated 2.2% in men and 5.5% in women in all age groups, whereas it was 30% when detected by clinical assessment (13). Based on nerve conduction studies, the rate of functional impairment among children with diabetes was 28% to 58% (14, 15). Since the prognosis of complications among these patients is critical, annual pediatric and adult screening for the early diagnosis of DN is recommended by international guidelines (16). Bedsides, the diagnosis of diabetic peripheral neuropathy (DPN) in young patients are performed via a simple and inexpensive method that incorporates diapason, lukewarm water, and examination of ankle jerk reflex. Through this approach, it is possible to diagnose PN in early stages, which contributes to metabolic control and prevents severe complications such as amputation and foot ulcer (17). Considering the importance of timely diagnosis of PN and reduction of the severity of the disease complications, we aimed to determine the prevalence of PN and its related factors in children with type 1 diabetes presenting to the endocrinology clinic of Neyshabur city, Khorasan Razavi province, Iran.

2- MATERIALS AND METHODS

2-1. Study design and population

This cross-sectional study was conducted among Diabetic children who visited the pediatric endocrinology clinic of Neyshabur city, Iran, in 2016. Overall, we enrolled sixty children who were selected by convenience sampling method.

2-2. Methods

In this study, diabetes was diagnosed based on A1C, fasting blood glucose (FBG), and oral glucose tolerance test (OGTT). All the diabetic children were receiving insulin therapy. The treatment was performed to control symptoms, maintain normal growth, maturation, and normal blood lipids, and minimalize urinary glucose loss. The

routine clinical methods were adopted for the measurement of conduction velocities. First, baseline characteristic including age, gender, diabetes duration, weight, stature, and family history of diabetes were recorded in a research- made-questionnaire. All the children were examined for the presence or absence of PN by an endocrinologist. Subjective neuropathic symptoms and neurological assessment results were assessed in all the children endocrinology clinic of Neyshabur city (Iran). Clinical examination was carried out for each patient by assessing the vibration sense using a 128-Hz tuning fork. Neurological examination, including pain and thermal sensation, deep reflux, fine touch, pinprick, and knee reflex test, was performed for each child.

Peripheral vascular examination was also performed by evaluating dorsalis pedis and posterior tibial pulses. A score of zero was considered in the presence of pain and thermal sensations and vibration of each of the legs and a score of one was given in the case of absence or reduction of these senses. In the Achilles reflex test, a score of one was assigned in the case of reduction of this reflex and zero was given if this reflex was normal. In addition, a score of two was assigned in the absence of Achilles reflex for each leg. Therefore, the scores within the range of 3-5 were considered as mild PN, while the scores 6-8 and 9-10 was considered as moderate and severe PN, respectively (18).

2-3. Ethical consideration

In accordance with the ethical principles, we obtained the approval of the Ethics Committee of Neyshabur University of Medical Sciences. Furthermore, we obtained written informed consent from all the participants. Additionally, the participants were assured of the confidentiality of their information and the possibility of withdrawal from the study at any time.

2-4. Inclusion and exclusion criteria

The inclusion criteria consisted of diagnosis of type 1 diabetes, age between older than 20 years old, and disease duration of more than three years. The exclusion criteria were diagnosis of underlying chronic diseases, mental retardation, or psychiatric diseases

2-5. Data Analyses

To analyze the data, Chi-squared test was run using SPSS software (version 16.0). P-value less than 0.05 were considered statistically significant.

3- RESULT

We aimed to determine the prevalence of PN and its related factors in children with type 1 diabetes. The mean age of the children was 10.8±3.38 years (age range: 3-18 years). The age of 3.4% (n=2) of the participants was less than 6 years and 8.6% (n=5) of them were older than 15 years. Further, 46.6% (n=27) of the children were aged between 6 and 10 years, and 41.4% (n=24) of them were within the 11-15years age group. About, 43.3 % (n=26) of the patients were male and 56.7% (n=34) of them were female. Moreover, 8.5% (n=4) of the children were offspring of consanguineous marriages. Also, 5.4% (n=2) of the children had family history of diabetes. The mean of weight, birth weight, height; body mass index (BMI), fasting blood sugar (FBS), duration of diabetes, and HbA_{1C} shown in **Table.1**.

Urine protein (albumin) was observed in three patients. The assessment of FBS showed that nearly 14.5% (n=14) of the children were normal and 74.6% (n= 46) of them had diabetes. The assessment of HbA_{1C} (lower than 7 mmol/L) showed that about 69% (n=49) of the children were normal and 31% (n=11) of them had diabetes. Based on bedside scoring procedure, 55% of the patients did not have DPN. The DPN score was moderate in 6.7% of the children and it

was mild in 38.3% of them. Overall, 23% of the children who had HbA_{1C}exceedingthe normal range had PN. In this study, except for FBS (P=0.13), and HbA_{1C} (P=0.59), the distribution of other variables was abnormal (P>0.05). The status of PN based on age, gender, BMI, duration of diabetes, FBS, and HbA_{1C}ispresented in **Table.2**. The assessment of degree of DPN based on age and gender showed no significant differences among the participants (Chi-square test (χ^2) = 8.88, P=0.18 and χ^2=2.62, P=0.26, respectively). The assessment of DPN based on duration of diabetes indicated a significant difference among the participants (χ^2=50.9, P=0.05). The study of BMI score based on various degrees of DPN showed no significant difference among the subjects (χ^2=0.76, P=0.68). The study of HbA_{1C} rate based on different degrees of DPN showed a significant difference (χ^2=18.72, P=0.001). Also, FBS score was significantly different between the children with DPN and those without it (χ^2=12.26, P=0.01).

Table-1: The means of weight, birth weight, height, body mass index, fasting blood sugar, duration of diabetes, and HbA_{1C} in Diabetic Children.

Variables	Mean (SD)	Minimum	Maximum
Weight (kg)	35.04 (24.95)	12	199
Birth weight (gr)	3069.12 (615.74)	140	4100
Height (cm)	157.30 (184.34)	15	1463
BMI (kg/m)	16.69 (4.23)	12	41
Fasting blood sugar (mg/dl)	134.13 (52.55)	10	363
Duration of diabetes (month)	34.89 (32.88)	4	144
HbA_{1C} (mmol/mol)	8.99 (1.419)	5.3	12.7

BMI: Body mass index; SD: Standard deviation; HbA1C: Hemoglobin A1C.

Table-2: The status of peripheral neuropathy based on age, gender, body mass index, duration of diabetes, fasting blood sugar, and HbA_{1C} in Diabetic children.

Variables		Without PN	Mild PN	Moderate PN	Chi-square test	P-value
Age (years)	<6	6.5%	0	0	8.88	0.18
	6-10	58.1%	30.4%	50%		
	11-15	32.3%	56.5%	25%		
	16-20	3.2%	13%	25%		
Gender (%)	Male	44.4%	50%	0	2.62	0.26
	Female	55.6%	50%	100%		
Duration of diabetes (month)	<36	75.8%	69.6%	50%	50.9	0.05
	36-72	21.2%	13%	50%		
	>72	3%	17.4%	0		
BMI (kg/m)	Thin	85.7%	81%	66.7%	0.76	0.68
	Normal	14.3%	19%	33.3%		
	Overweight	0	0	0		
HbA_{1C} (mmol/L)	Normal	87.9%	39.1%	100	18.72	0.001
	Diabetic	12.1%	60.9%	0		
FBS (mg/dl)	Normal	15.6%	14.3%	0	12.26	0.01
	Diabetic	84.3%	85.7%	100%		

PN: Peripheral neuropathy, FBS: Fasting blood sugar, BMI: Body mass index; HbA1C: Hemoglobin A1C.

4- DISCUSSION

In general, our findings showed that DPN was diagnosed in 23% of children with diabetes and those in the pre-diabetes stage. The assessment of HbA_{1C} and FBS based on different degrees of DPN showed that the rate of these variables was higher in children with DPN. In addition, duration of diabetes was longer in children with mild and moderate DPN. The role of HbA_{1c} is emphasized as an index of glycemic control and it is known as a risk-factor for DN (19). However, some studies reported conflicting results (15). It seems that efficient blood glucose control is effective in DN prevention (19). Intracellular metabolic changes that hinder nerve function may lead to DN. DN is also caused by nerve ischemia from microvascular disease and effects of hyperglycemia on neurons. Based on the studied nerves, deep peroneal and sural nerves are found to be the most commonly affected nerves in DPN. Patients with DPN have shown some complications. Variable degrees of sensory loss, numbness, large myelinated nerve fiber dysfunction, impairment in pain or thermal sensation are reported as DN complications (20, 21).

Although hyperglycemia plays an important role in the development of DN, neuropathy can occur in the absence of hyperglycemia (22). The rate of DPN among children with DM was assessed in one study by Hasani et al. Based on that study, DM complications were observed in one-third of patients, 62.5% of which were subclinical. This rate is higher than our results, but this difference is not significant(20). Based on one study by Chen et al., overall prevalence of DPN was 33.1% in patients with Type 2 diabetes (19). According to in Ghorbani et al., sensorimotor polyneuropathy is observed in 77.4% of diabetic patients (type II) (23). It is suggested that 1.3% of the population have some type of clinically recognized DM, 27% of whom have type 1 DM mostly diagnosed through neuropathy (24). DN in children is not severe enough to present definite or readily observable symptoms; therefore, its estimation is not accurate, but it is not uncommon in this age group, such that its pathological findings in the distal nerves have been reported in one-fourth of young patients with type 1 DM (25). Similar to our study, bedside scoring system was used to diagnose DN in young patients with type 1 diabetes in a study by Shalitin et al. Based on the mentioned study, the prevalence of DN was 17.1% and it is associated with long-term glycemic control, duration of diabetes, duration of diabetes after puberty, and the presence of retinopathy and proteinuria (17).

Based on another study, the prevalence of DN was reported 13.75% (26). In our study, the duration of diabetes was longer in patients diagnosed with DPN, such that diabetes duration was five years or longer in one-fifth of patients, 45.1% of whom showed mild and moderate DN. Similar to our study, in a study conducted by Hasani et al., electrophysiological evidence was reported in 45% of the patients with diabetes duration of five years or longer (20). This was estimated 57% in Canadian children with type 1 DM duration of at least five years (15).

Although the relationship between diabetes duration and the presence of DPN is rejected in some studies (27), it is introduced as a major factor in developing DPN in many studies (28-31). Therefore, further studies in this regard are recommended. In our study, diabetes duration was less than one year in 13% of the children, which was 15.8% in the study by Hassani et al. (20). Some studies showed that the fastest deterioration of nerve function occurred early after the onset of type 1 DM (within 2-3 years), while its progression is at a slower pace (32). Based on nerve conduction studies, abnormal findings were found in25%

patients who were newly diagnosed with pediatric diabetes (29).

4-1. Limitations of the study

The main limitations of this study were the limited sample size, as well as lack of kit in Neyshabur labs and assessment of prevalence of peripheral neuropathy in other types of diabetes. Moreover, the assessment of children aged less than five years was impossible. Therefore, we recommend further larger studies assessing the prevalence of PN in diabetic children in this age group.

5- CONCLUSION

In summary, our study showed that 23% of children with diabetes have DPN. Also, the duration of diabetes was a main factor in causing PN. Therefore, neurological assessment including nerve conduction studies and meticulous physical examination should be performed for evaluating the function of large sensory and motor fibers. Neuropathy as a major complication of insulin-dependent diabetes mellitus in adults and children should be seriously assessed. Since it affects both the peripheral and autonomic nervous systems, patients with diabetes can show early evidence of neuropathy. For this reason, the assessment of complications associated with the metabolic effects of insulin deficiency on the various constituents of the peripheral nerve is recommended in future studies.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENTS

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