

**Diabetic neuropathy in children (Article Review)**

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**Abstract:**

Diabetes mellitus is one of the most common chronic diseases in children , and more than 90% of all diabetes cases in childhood is type 1 diabetes mellitus (T1DM). Several complications, including retinopathy, diabetic kidney disease, hypertension, cardiovascular autonomic, and peripheral sensory neuropathy, are associated with the onset of diabetes in childhood and represent a significant burden for the health care system. Diabetic autonomic neuropathy was defined as an autonomic nervous system disorder in diabetes or prediabetes after the exclusion of other causes, while diabetic peripheral neuropathy as a “symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and microvessel alterations as a result of chronic hyperglycemia exposure (diabetes) and cardiovascular risk covariates.

**Key words:**

**Introduction: Diabetes mellitus, children, neuropathy. Introduction:**

Childhood diabetes has many forms including rare conditions, such as, neonatal diabetes, chronic disease associated (e.g. with cystic fibrosis) and monogenic diabetes (e.g. maturity onset diabetes of the young). The most common forms of diabetes are, Type 1 and Type 2 diabetes [1].

Insulin-dependent diabetes mellitus (IDDM), type 1 diabetes (T1DM), is a classic example of a T cell-mediated autoimmune disease characterized by selective destruction of pancreatic  $\beta$  cells leads to increased blood sugar levels [2,3].

The reported incidence of childhood T1DM differs from 0.1 to 40.9 per 100,000 annually worldwide and the rate is increasing over time. The majority of children with diabetes present between 10 and 20 years of age [4–6].

Diabetic neuropathy (DN) is a major complication of T1DM. This term usually points to polyneuropathy and can be categorized into two broad subclinical and clinical stages [7].

It is the commonest form of neuropathy and may affect about half of all patients with diabetes (DM), causing considerable morbidity and mortality and resulting in a giant economic burden [8]. Diabetic neuropathy refers to the presence of symptoms and/or signs of peripheral nerve dysfunction due to diabetes [9].

Type 1 diabetes mellitus (T1DM) is a chronic immune-mediated disease, in which the pancreas ceases to produce enough insulin (10). The overall increase in the incidence of T1DM was estimated at nearly 3%, and the annual incidence of this condition varied from 0.61 cases per 100000 populations in China to 57.6 cases per 100000 in Finland (11). Middle East region, Saudi Arabia and Kuwait have the highest incidence rate at 31.4 and 22.3/100000 per year (12).

Annually, 1 to 35 new cases of T1DM (younger than 14 yr) per 100000 populations are diagnosed per year. In various countries, the incidence rate of T1DM has at least doubled over the past two decades. The incidence of this condition seems to raise as the distance from the equator increases (13).

Peripheral nervous system involvement is a common complication of T1DM, and unlike adults, patient's polyneuropathy has no clinical manifestations in diabetic children (14). The prevalence of neuropathy varies depending on the severity and duration of hyperglycemia (10). The prevalence of peripheral neuropathy in both adults and children ranges between 7% and 57% (15).

Nerve conduction velocity (NCV) test is the method of choice for the diagnosis of neuropathy. The incidence of neuropathy in different studies ranges from 10% to 68% among diabetic patients (16).

Pediatric neuropathy attributed to metabolic dysfunction is a well-known complication in children and youth with type 1 diabetes. Moreover, the rise of obesity and in particular of type 2 diabetes may cause an uptick in pediatric

neuropathy incidence. However, despite the anticipated increase in neuropathy incidence, pathogenic insights and strategies to prevent or manage neuropathy in the setting of diabetes and obesity in children and youth remain unknown. Data from adult studies and available youth cohort studies are providing an initial understanding of potential diagnostic, management, and preventative measures in early life. (17-20).

Diabetic neuropathy is a type of nerve damage that can occur if you have diabetes. High blood sugar (glucose) can injure nerves throughout the body. Diabetic neuropathy most often damages nerves in the legs and feet.(22-26)

Depending on the affected nerves, diabetic neuropathy symptoms include pain and numbness in the legs, feet and hands. It can also cause problems with the digestive system, urinary tract, blood vessels and heart. Some people have mild symptoms. But for others, diabetic neuropathy can be quite painful and disabling.(27)

Diabetic neuropathy is a serious diabetes complication that may affect as many as 50% of people with diabetes. But you can often prevent diabetic neuropathy or slow its progress with consistent blood sugar management and a healthy lifestyle.(28-31)

Diabetic neuropathy refers to the presence of symptoms and/or signs of peripheral nerve dysfunction due to diabetes (32). Other potential causes, such as vitamin deficiency, infection, inflammatory, toxic, metabolic, autoimmune, paraneoplastic, or inherited neuropathy, should be excluded (16). DN is generally subdivided into generalized symmetric or focal asymmetric forms of neuropathy. The most common type of childhood DN is a distal symmetric polyneuropathy (33).

Diabetic DSP is a neurodegenerative condition caused by metabolic and vascular insults (34) to the peripheral nerves, mediated via a number of mechanisms, including:

(1) increased activity of the polyol and hexosamine pathways;

- (2) depletion of myoinositol;
- (3) reduced activity of Na/K ATPase;
- (4) increased sorbitol levels;
- (5) reduced nerve growth factors;
- (6) increased free oxygen radicals (35).

Peripheral neuropathy is a heterogeneous group of diseases characterized by peripheral nerve damage. Associated signs and symptoms include sensory loss, paresthesia, and pain.<sup>1-3</sup> Numerous inherited and acquired causes of peripheral neuropathy manifest in children and youth.<sup>2-4</sup> Inherited forms include Charcot-Marie-Tooth disease and inherited metabolic disorders, such as Fabry disease, Leigh syndrome, and metachromatic leukodystrophy.<sup>4-6</sup> Acquired neuropathy can occur with diabetes, infectious disease, toxin exposure, vasculitis, compression/trauma, vitamin deficiencies, and immune-mediated disorders.<sup>(34)</sup>

While peripheral neuropathy in children and youth is primarily due to hereditary causes, diabetes is increasingly reported as the cause of neuropathy in children and youth. Type 1 diabetes (T1D) accounts for about 98% of all diabetes cases younger than 10 years and 87% of all diabetes cases in adolescents (aged 10–19 years).<sup>(23)</sup> As the prevalence of T1D and type 2 diabetes (T2D) is rising among this demographic,<sup>(23)</sup> the incidence of pediatric diabetic neuropathy (DN) is also increasing. Moreover, the lifetime exposure to diabetes is longer in subjects diagnosed in early life.<sup>9</sup> Given that diabetes complications emerge with disease longevity, the increasing diabetes rates in children and youth is alarming since many will be at risk of diabetes complications in early adulthood.<sup>14</sup> Longstanding, poorly controlled diabetes is a well-established DN risk factor.<sup>(36,37)</sup> Recent data, however, implicate risk factors beyond hyperglycemia for childhood onset DN.

## **Classification of Diabetic neuropathy:**

Diabetic neuropathy can be classified into 4 subgroups:

- Proximal neuropathy/ diabetic amyotrophy.
- Peripheral neuropathy / diabetic nerve pain / distal polyneuropathy.
- Autonomic neuropathy.
- Focal neuropathy / mononeuropathy.

## **Management**

Medical management starts with Optimized glycemic control (mainly for type 1 DM) and lifestyle interventions (38). Lifestyle intervention includes physical exercise and weight loss.

Tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (e.g. duloxetine) and anticonvulsants (e.g. pregabalin and gabapentin) are commonly prescribed treatments for neuropathic pain . At present, there are no universally accepted disease modifying medicines, but this is currently being researched and developed (39,40)

Moreover, multidisciplinary team management is required for the prevention and management of diabetic foot complications

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