

# DIABETIC NEUROPATHY AND ITS TREATMENT: A NEUROLOGICAL DISEASE.

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**Abstract:** Diabetic peripheral neuropathy (DPN) may be a common chronic complication of diabetes mellitus. It results in distressing and expensive clinical sequelae like foot ulceration, leg amputation, and neuropathic pain (painful-DPN). Unfortunately, DPN is usually diagnosed late when irreversible nerve injury has occurred, and its first presentation is also with a diabetic foot ulcer. Several novel diagnostic techniques are available which can supplement clinical assessment and aid the first detection of DPN. Moreover, treatments for DPN and painful-DPN are limited. Only tight glucose control in type 1 diabetes has robust evidence in reducing the danger of developing DPN. However, neither glucose control nor pathogenetic treatments are effective in painful-DPN and symptomatic treatments are often inadequate. It's recently been hypothesized that using various patient characteristics it should be possible to stratify individuals and assign them targeted therapies to provide better pain relief. We review the diagnostic techniques which can aid the first detection of DPN within the clinical and research environment, and recent advances in precision medicine techniques for the treatment of painful-DPN.

**Keywords:** Diabetes mellitus (DM), Diabetic peripheral neuropathy (DPN), Sensory, Motor, Autonomic

## INTRODUCTION

### A. Diabetic Neuropathy and diabetes.

Diabetic neuropathy (DN) is a chronic and progressive disease occurred in central nervous system and peripheral nervous system. It is characterized by nerve damage due to hyperglycaemia in extracellular space. The major symptoms of the disease can be characterized as positive and negative symptoms. Loss of sensation, weakness and numbness are a negative symptom. Tingling, burning, and stabbing pain are a positive symptom. Diabetes is that the commonest reason for peripheral neuropathy worldwide. Diabetic neuropathy represents a heterogeneous group of syndromes with clinical and subclinical disorders and abnormalities like distal symmetrical polyneuropathy, Mononeuropathy, diabetic amyotrophy, autonomic dysfunction, or cranial neuropathies. The pathogenesis and underlying mechanisms leading to diabetic neuropathy are complex and not yet fully known. Regarding the nerve cells, both large and small nerve fibres is also involved within the course of the disease DPN is related to increased mortality and ends up in morbidity, principally as a result of its two major clinical consequences, diabetic foot ulceration, and neuropathic pain. Diabetic foot ulceration occurs as a result of a posh interaction of risk factors and patient behaviours, but sensory loss secondary to DPN is most frequently the first cause. Although DN is an umbrella term encompassing a range of clinical manifestations, most psychosocial research to date has targeting neuropathic pain and foot ulceration. While our review reflects this pattern, it also emphasizes the importance of other clinical presentations of DN. Postural instability, as an example, although not often mentioned in older texts, is one in every of the strongest predictors of depression. Whereas neuropathic pain contributes to depression, it's postural instability and its psychosocial consequences that dominate this relationship over time. [1, 3, 5, 10]

Small fibers damage often occurs early in diabetes and leads patients to hunt medical assistance before DM is diagnosed. C-nociceptive unmyelinated fibres are affected in an early stage of the disease, presenting with pain, allodynia, and hyperalgesia. Large fibre neuropathies include sensory and motor nerves and manifest by reductions in sensitivity to touching, vibration and position, still as weakness, muscle wasting and diminished or absent deep tendon reflexes. The prevalence of diabetes, DPN and foot amputations still increase at an alarming rate. it's essential that the condition is diagnosed early and accurately so that measures could also be implemented to cut back the danger of diabetic foot complications. Number of differences are discovered between painless- and painful-DPN, the specific mechanisms causing the condition are unknown Disease modifying treatments don't seem to be widely used for painful-DPN and therefore the treatment remains largely symptomatic. Unfortunately, the available treatments for neuropathic pain are often ineffective and poorly tolerated. Importantly, most DPN-related amputations are preventable. 80% of those amputations may be prevented. [11,13,14] through good multidisciplinary care, which not only reduces amputation risk, but also substantially reduces the rates of hospitalisation and re-ulceration.3 Notably, the relative likelihood of death within 5 years following a lower-limb amputation secondary to a diabetic foot ulcer is greater than for prostate and carcinoma. [15]

## B. Classification and Definition of Diabetic.

Diabetic neuropathies are heterogeneous in their clinical presentation, risk factors and pathophysiology. The neuropathic syndromes may be classified according to the nerve type affected (sensory vs. motor vs. autonomic), site of nerve injury (focal vs. multi-focal vs. generalized), and disease time course (acute vs. chronic).

### A. Diffuse neuropathy

#### DSPN

- Primarily small-fibre neuropathy
- Primarily large-fibre neuropathy
- Mixed small- and large-fibre neuropathy (most common)

#### Autonomic

- Cardiovascular: Reduced HRV, Resting tachycardia, Orthostatic hypotension, Sudden death (malignant arrhythmia)
- Gastrointestinal: Diabetic gastroparesis; Diabetic enteropathy (diarrhoea). Colonic hypomotility (constipation)
- Urogenital: Diabetic cytopathy (neurogenic bladder), Erectile dysfunction, Female sexual dysfunction

#### Sudomotor dysfunction

- Distal hyperhidrosis/anhydrosis
- Gustatory sweating
- Hypoglycaemia unawareness
- Abnormal pupillary function

### B. Mononeuropathy (Mononeuritis multiplex) (atypical forms)

- Isolated cranial or peripheral nerve (e.g., CN III, ulnar, median, femoral, peroneal)
- Mononeuritis multiplex (if confluent may resemble polyneuropathy)

### C. Radiculopathy or polyradiculopathy (atypical forms)

- Radiculoplexus neuropathy (lumbosacral polyradiculopathy, proximal motor amyotrophy)
- Thoracic radiculopathy

Diabetic nerves reveal a paradoxical contrast between their physiologic resistance to ischemia and increased morphologic susceptibility to ischemia. Diabetic nerves are particularly prone to reperfusion injury. Diabetic subjects, therefore, may suffer from severe neuropathic damage even after normally tolerable ischemia and reperfusion. The explanation of painful DPN is additionally dependent on whether the patient has type 1 or type 2 diabetes[11]. In type 2 diabetes, painful neuropathic signs or symptoms can be present at diagnosis or before the diagnosis of diabetes. Currently it's uncertain whether this results from a chronic period of undiagnosed diabetes or impaired glucose tolerance, or due to a separate mechanism that results from the altered metabolic milieu, perhaps resulting from hypertriglyceridemia or thus far unstudied effects of obesity. Neuropathy within the patient with type 1 diabetes is said to duration of diabetes. [1, 8, 11, 14]

## C. Sign and symptoms OF DPN

The symptoms are predominantly sensory and might be classified as “positive” (tingling, burning, stabbing pain, and other abnormal sensations) or “negative” (sensory loss, weakness, and numbness). Motor symptoms are less common and occur later within the disease process. Decreased sensation within the feet and legs confers a predisposition to painless foot ulcers and subsequent amputations if the ulcers aren't promptly recognized and treated, particularly in patients with concomitant peripheral artery disease. The lifetime risk of a foot lesion, including an ulcer or gangrene, in persons with distal symmetric polyneuropathy is 15 to 25%.1 additionally, sensory loss, combined with loss of proprioception, results in imbalance and unsteadiness in gait, increasing the likelihood of a fall which will end in lacerations, fractures, or traumatic brain injury. [15,12] Some persons with distal symmetric polyneuropathy could also be asymptomatic, and signs of disease is also detected only by means of a close neurologic examination. [5]

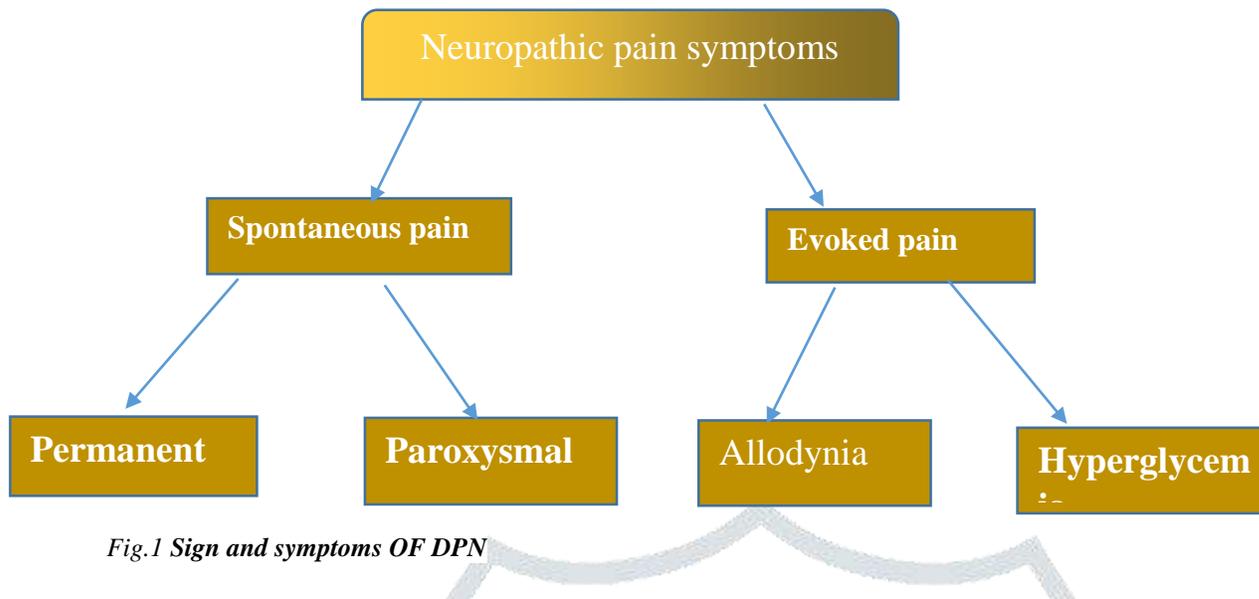


Fig.1 Sign and symptoms OF DPN

The symptoms of painful diabetic neuropathy (PDN). [5]

1. Permanent. (Superficial burning, Deep compression)
2. Paroxysmal. (Electric shock, Shooting-like sharp)
3. Allodynia. (Dynamic (soft skin brushing), Static (light pressure), Thermal (warm – cold))
4. Hyperglycemia. (Hot, Cold, Pinprick)

#### A. Risk Factors of DPN.

Age, obesity, smoking, hypertension, dyslipidemia, and peripheral artery disease are associated with an increased risk of pain. A motivating observation in type 2 diabetes is that the event of DPN is also related to chronic hyperglycemia, and yet painful DPN is not explained by this. Think about comparison with painless DPN [4,3,10]. When considering the relative importance of the danger factors for developing painful DPN, it should be that they'll only be applied to type 2 diabetes; because the majority of the topics with painful DPN in epidemiologic studies have had type 2 diabetes. It should be vital to seem specifically at the risk factors that influence the event of DPN in type 1 diabetes, as there are some aspects of the clinical presentation and explanation that time to the existence of different pathologic mechanisms for painful DPN in type 1 diabetes [14,5,9,14].

#### B. Pathophysiology/Pathogenesis of DPN

DPN results in degenerative and atrophic changes throughout the peripheral and central nervous system. The peripheral end terminals of nociceptors, intra-epidermal nerve fibers, are depleted in an exceedingly distal symmetrical manner in DPN. More proximally, peripheral nerve changes are well described and include; demyelination of myelinated nerve fibers, axonal degeneration and necrosis, Schwannopathy, and microangiopathy. Furthermore, autopsy and newer advanced imaging studies have found funiculus and cerebral atrophy related to DPN. An exact understanding of the pathophysiology of DPN remains elusive. Variety of molecular pathways correlate with functional nerve impairment and pathological neuronal changes, including, but not limited to: polyol pathway activation, oxidative stress, protein kinase C activation, and advanced glycation consequence formation. [15] However, the precise causal links between hyperglycemia and clinical DPN is uncertain. Our current understanding is that hyperglycemia, likewise as vascular risk factors, activate detrimental pathways ultimately resulting in downstream injury to the micro vessel endothelium, nerve support cells, and nerve axons. Recent advances suggest that the cumulative effect of those injurious events may cause neuronal death via reactive oxygen species generation and mitochondrial dysfunction. Furthermore, mechanistic and pathological findings don't discriminate between painful- and painless-DPN

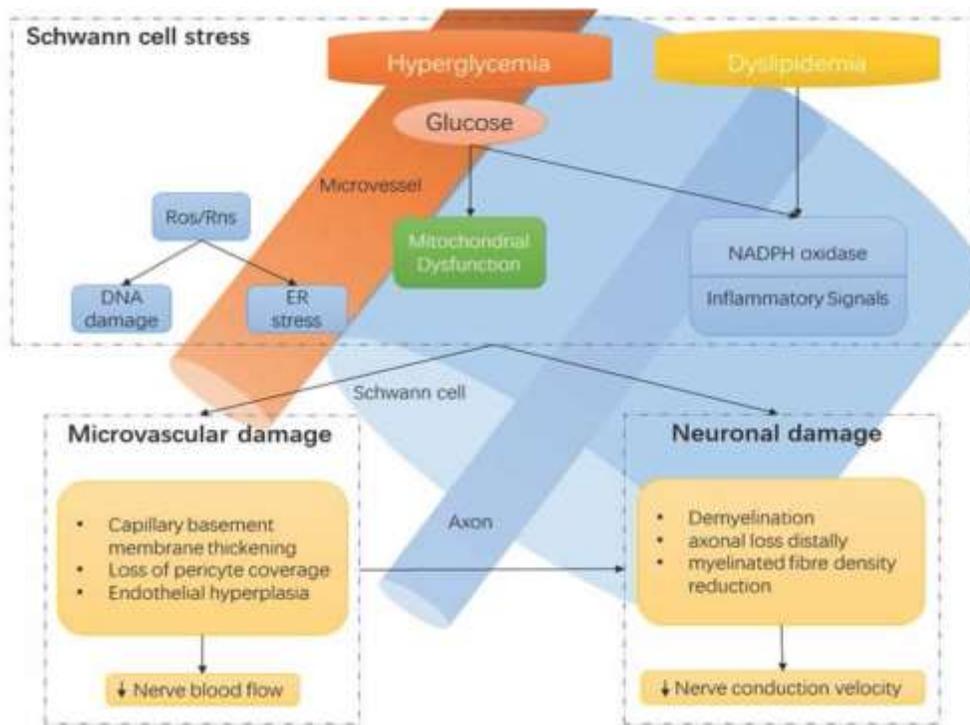


Fig. 2 Hyperglycaemia-driven Schwann cell stress and neuronal damage. Hyperglycaemia and dyslipidemia lead to reduction of neuronal support from Schwann cells and micro vessels. Disruption of neuronal support by Schwann cells and the vascular system contributes to neuropathy, in conjunction with the direct effects of hyperglycaemia on neurons. ER, endoplasmic reticulum; NADPH, Nicotinamide adenine dinucleotide phosphate; Ros, reactive oxygen species; Rns, reactive nitrogen species. [13]

### C. Pharmacological Treatment of DPN

#### 1. Antidepressants.

Tricyclic and tetracyclic antidepressants (TCAs) have been found to be efficacious for several varieties of painful neuropathies. TCAs are serotonin/norepinephrine reuptake inhibitors. The various subtypes don't differ significantly in their efficacy. The consequences include blocking Na channels within the peripheral system (PNS) and alteration of serotonin and norepinephrine activity within the central nervous system (CNS) nociceptive-modulation system. Many studies have shown the efficacy of TCAs compared to placebo. The analgesic effect of TCAs seems to occur at the synaptic level by increasing the bioavailability of serotonin and norepinephrine, which are able to inhibit effects of the nociceptive pathway. These neurotransmitters are involved in two descending inhibitory pathways located in the brainstem and medulla spinalis. [3, 7, 4] Amitriptyline was evaluated in an exceedingly double-blind, randomized crossover trial by Max (1992) in 29 patients with painful diabetic neuropathy. The patients received 25 mg amitriptyline at bedtime, titrated to the utmost tolerated dose (150 mg/day) over 3 weeks. the ultimate dose was maintained for one more 3 weeks. Amitriptyline was compared against a full of life placebo, a mixture of diazepam and benztropine to mimic the adverse effects. Amitriptyline (150 mg/day) showed a benefit compared to placebo and therefore the pain reduction wasn't correlated with improvement in mood. the foremost common side-effects were waterlessness, sedation, dizziness, and constipation. [4] Desipramine (111 mg/day) is healthier tolerated than amitriptyline and showed the identical positive effect. Furthermore, it's the smallest amount anticholinergic and sedating side-effects compared with the primary generation tricyclic antidepressants. Desipramine can be another for patients unable to tolerate amitriptyline. [7]

#### 2. Anticonvulsants

Gabapentin and pregabalin are  $\alpha 2\delta 2$  voltage-gated calcium modulators that are frequently accustomed treat painful diabetic neuropathy. These agents relieve pain by means of direct mechanisms and by improving sleep. 27,28 In contrast to gabapentin. Pregabalin has linear and dose-proportional absorption within the therapeutic dose range (150 to 600 mg per day); it also contains a more rapid onset of action than gabapentin and a more limited dose range that needs less adjustment. Gabapentin requires gradual adjustment to the dose that is usually clinically effective (1800 to 3600 mg per day). [3, 7, 4] Topiramate has also been shown to reduce the intensity of pain and to enhance sleep; studies indicate that it stimulates the expansion of intraepidermal nerve fibers. Unlike pregabalin and gabapentin, which may cause weight gain, topiramate causes weight loss, which has been amid improvements

in lipid levels and pressure and increases within the density of intraepidermal nerve fibers of 0.5 to 2.0 fibers per millimeter each year, as compared with a decline of 0.5 to 1.0 fibers per millimeter per year in untreated patients. [3]

### 3. Opioid Analgesic

Opioids is also effective within the treatment of neuropathic pain caused by distal symmetric polyneuropathy. However, given the attendant risks of abuse, addiction, and diversion, opioids should generally be used only in selected cases and only after other medications have didn't be effective. Tramadol, an atypical opiate analgesic, also inhibits the reuptake of norepinephrine and serotonin and provides effective pain relief. This drug also contains a lower potential for abuse than other opioids. Extended-release tapentadol has similar actions and has been approved for the treatment of diabetic neuropathic pain by the Food and Drug Administration. In one study, the combined use of gabapentin and sustained-release morphine achieved better analgesia at lower doses of every drug than the use of either drug alone but was amid an increase in adverse effects, including constipation, sedation, and xerotes. [3, 7, 4]

### 4. Tramadol.

Tramadol, as an m-receptor agonist, may also stimulate the serotonergic and noradrenergic systems. in an exceedingly randomized, double-blind, placebo-controlled study, tramadol at a dose between 200 and 400 mg per day over 6 weeks reduced pain, paresthesia and touch-evoked pain in DPN compared to placebo. Another trial, examining the benefit of a mixture therapy with 37.5 mg tramadol and 325 mg acetaminophen (APAP) over 66 days, reported an improvement compared to placebo. Tramadol may be an alternate to other opioids. Nevertheless, its use is limited by its side-effects like nausea, constipation, headache, or dyspepsia. [3, 7, 4]

### 5. Antiepileptics

Antiepileptics regulate neuronal excitability at the synaptic level; this became the impetus to explore other indications for their use beyond epilepsy. Phenytoin was one in all the primary non-sedating, sodium channel antagonists available for treating epilepsy. Phenytoin also has the power to dam L-type mediated Ca current, inhibit NMDA response, depress basal intraneuronal levels of cyclic guanosine monophosphate, and increase neuronal GABA concentration. During the 1970s, phenytoin was tested as a treatment in painful DPN. Lack of efficacy and severe side-effects, however, prevent phenytoin from being employed as a primary line option for treatment of DPN. [3, 7, 4]

### 6. Nonsteroidal Anti-inflammatory Drugs.

Inflammatory responses accompany peripheral nerve injury, including the assembly of prostaglandins. Prostaglandin synthesis depends on cyclooxygenase (COX)-1 or COX-2. The prostaglandin-mediated pain is that the result of increased sodium currents and calcium influx in peripheral nociceptive nerve cells. Additionally, this reaction provides a release of central neurotransmitters and depolarization of second-order nociceptive neurons. Nonsteroidal anti-inflammatory drugs (NSAID) inhibit cyclooxygenase, and thus prostaglandin-mediated inflammation. Usually NSAIDs don't seem to be recommended for neuropathic pain therapy because of their side-effects (GI tract, renal, cardiac) and their questionable effect in neuropathic pain reduction. A review of NSAID use in neuropathic pain revealed a discrepancy in the widespread use of NSAIDs by patients with neuropathic pain and also the belief among pain specialists of the lack of efficacy. There are studies indicating efficacy of NSAID therapy in neuropathic pain in animal models, but not in human conditions. However, other studies have didn't demonstrate a difference between NSAIDs and placebo. Currently there's insufficient evidence to recommend NSAIDs for the treatment of neuropathic pain and NSAID use might not be appropriate for those patients with diabetic nephropathy. [3, 7, 4]

## ***D. Non Pharmacological Treatment of Diabetic Neuropathy***

### 1. Natural Methods for Controlling DM

**Diet;** The patients who are diabetic not be ready to eat normally are a myth. Paleolithic diet should be followed which incorporates fish, nuts, vegetables, and seeds show some glucose tolerance. Indians were recommended with new dietary guidelines by the diabetes foundation by considering some important factors like calorie intake as per weight, calculation of ideal weight, and number of servings for various food groups. A diabetic patient should never skip breakfast and may definitely have three meals and one or two snacks every day. Just in case of gestational diabetes in women, therapeutic lifestyle changes (TLC) diet which should be followed by the diabetic patients with abnormal cholesterol levels. TLC diet includes 25% of total fat consumption. Foods with

artificial sweeteners like aspartame, acesulfame-potassium, saccharine, and sucralose should be avoided as they have an inclination to accumulation of fats within the body.

### A. Carbohydrates and sweeteners.

Carbohydrate intake affects blood sugar levels. Thus, carbohydrate foods with lower glycemic index like starchy food like whole meal parts and whole grains, pulses, rice or wild rice, and brown bread are to be selected. Breadstuff, oatmeal, and pastries are to be avoided. Prefer green leafy vegetables rich in fiber; avoid carbohydrate-rich fruits like apple and fleshy fruits because they contain fructose. When sudden hypoglycemic condition was observed in patient with diabetes, low ceiling carbohydrates like breadstuff and cereals bananas are advisable. Avoid sugar drinks because they increase blood sugar levels. Instead prefer sugar-free or low sugar quenchers and fizzy drinks in minute quantity. Within the dietary management of type-II diabetes, low carbohydrate intake, i.e., 30 g/day is advisable. In vegetarians, the incidence of diabetes is low. Thereby vegetarian diet is more practical just in case of type-II diabetes and obesity. Timing of food intake plays a vital role within the management of diabetics. Rather than salt, prefer herbs and spices to flavor the food if necessary. To regulate diabetes in a very better way, take limited intake of calories in five diets serving method like breakfast, mid-meal, mid-day, evening, and dinner which comprises 3-h gaps between each serving. To balance the diet, prefer fruits and vegetables which are rich in vitamins and fibers a day. Fibrous strands admixed with flesh containing fruits like citrus fruits don't increase the blood glucose level just in case of moderate intake. [36-40] Methi coffee, which might be prepared with dried fenugreek seeds and wheat when added with milk, gives a coffee-like taste. Fenugreek seeds are one amongst the ingredients that help in decreasing the blood glucose level. [21] Diets with high glycemic index (GI), with high glycemic load (GL), or high altogether carbohydrates may predispose to higher blood sugar and insulin concentrations, glucose intolerance, and risk of type 2 diabetes. [24, 25] Regulation of blood sugar to realize near-normal levels could be a primary goal within the management of diabetes, and, thus, dietary techniques that limit hyperglycemia following a meal are likely important in limiting the complications of diabetes. [24, 25]

### B. Proteins.

It prefers plant-based proteins like beans, whole grains, and millets. Proteins <1 g/kg of weight are recommended just in case of patients without nephropathy. Just in case of patients with nephropathy, protein intake is restricted as they cause increased progression of failure. [28]

### C. Fats.

Fat consumption should be limited within the case of type-II diabetic patients because; obesity could be a major complication in them. Out of the overall energy consumption, the fat intake should be but <35%. Oils like oil and vegetable oil contain monounsaturated fats. But 10% of fats account for saturated and trans-unsaturated fats, and 10–20% accounts for monounsaturated fats. Palm oil, cocoa butter, milk products, and coconut are rich resources of saturated fats. Hydrogenated vegetable oils are rich source of trans-unsaturated fats so better avoid them. Sunflower-seed oil, corn seed oil, and soya bean oil are rich sources of N-6 polyunsaturated fats which accounts for 10% of energy intake and animal oil from fish which may be a rich source of N-3 Polyunsaturated fats should be eaten once or twice every week. Avoid butter, cheese, and margarine as they're high-fat content foods, prefer low-fat dairy products like low-fat yogurt, and milk. [21]

### D. Fibers.

About 50 g of soluble fiber produces improvement of 10% in fasting blood sugar, decreases beta-lipoprotein (LDL) and cholesterol just in case of a median person with NIDDM. The diet for diabetic patients should be comprised of rich amount of soluble fiber. Yams, winter squash, cauliflower mash, whole wheat pasta, whole grain bread, cold cereal, steel cuts oats, and gem are rich sources of fiber [26]

## 2. Surgery for Diabetes.

Obesity and sort 2 diabetes are serious chronic diseases that are related to complex metabolic dysfunction that ends up in systemic complications and increased mortality. Metabolic surgery is effective in improving type 2 diabetes in severely obese patients, often normalizing glucose levels and reducing or avoiding the requirement for diabetes medications. It's now recognized as a legitimate treatment option in appropriate patient populations. Surgery must be performed with a comprehensive long-term follow-up plan, including nutritional, behavioral and medical management. The mechanisms that facilitate the remission of diabetes, additionally to caloric restriction and weight loss, may include changes to incretin and peptide hormone levels, BAs and

gut microbiota. Ongoing research is required to define the relative contributions of those physiologic changes and to further improve long-term outcomes. [22]

### 3. Diabetic Stress Management.

Stress shows negative effects on patients with type-2 DM. The utility of stress management training shows conflicting evidence within the treatment of diabetics. Some studies reveal that the therapeutic effect of stress management has used time-intensive individual treatment [31]. It is often through with the implementation of behavioral stress management programs and also by the utilization of anxiolytics that reduce stress [30]. To enhance glycemic control in patients with uncontrolled type-2 DM, both the interventions are to be implemented carefully. Any style of stress either physical stress or mental stress may cause changes within the blood glucose levels, especially in diabetic patients. Not only the glycemic control is affected but it may cause complications like impaired physical and mental well-being, depression because of social relationships. Flight response of flight freeze is an evolutionary coping mechanism which makes the individual handle the harmful situation and threats. Many researchers found that top levels of stress may constantly spark to drastic changes on the wing freeze or flight response; this results in difficulty in controlling the blood sugar levels [29]

### 4. Diabetic Meditation.

Mindfulness meditation is that the art of creating awareness about this situation that has control of thoughts, emotions, and sensations which should be during a non-judgmental and accepting manner. Studies have shown that mindfulness meditation maintains glucose at stable levels in diabetics by accepting or acknowledging destructive emotion in an exceedingly non-judgmental way. [32, 33] Transcendental meditation could be a sort of meditation with a silent mantra. It involves the employment of mantra and meditates for 20 min twice daily. It mainly influences patients with type-2 diabetes. Insulin and glucose levels are increased by the strain hormone such adrenaline, noradrenaline, and cortisol. Transcendental meditation technique balances and reduces these hormones and helps regulation of glucose and insulin within the blood. [32, 33]

### 5. Exercise.

The DM patients need exercise which helps in reducing calories and fat deposition within the body. Intake of high-calorie food and lack of exercise causes complications like stroke and cardiovascular problems in diabetic patients. Exercise could be a well-known natural method of controlling diabetes. within the real sense, majority of the people assume heavy exercise like gymnastics and weight lifting are best exercises, small exercises like brisk walking, cycling are the foremost preferable exercises just in case of diabetic patients. By considering his/her health and physical status, the patient must select specific variety of exercise supported the necessity. Duration of exercise should depend upon physical acceptability and tolerability. During night after dinner, lying exercise is one among the most effective methods in diabetic patient who cannot listen for morning walk. This exercise is beneficial just in case of active foot diseases in uncontrolled diabetic patients. Avoid exercises within the sort of walking which can worsen the condition of the foot. [34]

### 6. Diabetic Yoga.

The main causes of diabetes are obesity, stress, lack of exercise, and genetic factors. The incidence of type-II diabetics are going to be more just in case of obese patients thanks to the body fat and fat circulating within the bloodstream which interferes with the flexibility of cells to use insulin. The level of estrogen and progesterone in our body may cause changes in blood glucose level, especially during the 3rd week of the oscillation. Most girls though don't notice this transformation. Obesity and diabetes may be considered as twin epidemics. By figuring the body mass index one can measure, whether the person is overweight or underweight or normal. The factors that cause obesity are genetically, environmental, and psychological. The persons who were adapted to a sedentary lifestyle are more susceptible to obesity. Drugs like steroids can cause weight gain in some patients. To facilitate the treatment for this twin epidemic adaptation, yoga lifestyle is more applicable [35]

### 7. Lifestyle Modifications in Diabetes

In certain conditions, increased blood sugar may cause diabetic retinopathy. Eye-care should be taken by consulting ophthalmologist. Daytime sleep should be avoided. Quit smoking and avoid alcohol. the chance of smoking in diabetes ends up in peripheral vascular disease which can led to amputation of toes, feet or legs, high cholesterol levels, and renal impairment which frequently ends up in dialysis, worsened blood glucose control compared thereto of in non-smokers with diabetes and even causes death especially because of stroke and coronary failure. Out of 100 patients newly diagnosed with diabetics, 25 patients are smokers. For the management of other comorbid disease conditions like high cholesterol level and high vital sign, prescription drugs should

be taken regularly without fail to forestall other new complications. Nicotine replacement therapy is suggested just in case of patients with diabetes to quit smoking. In healthy person, the results of smoking may be devastating, and just in case of diabetics, these effects are going to be worsened. The blood levels are going to be constricted, and also the cholesterol levels are increased thanks to smoking. It also often results in impotence. Avoid consumption of food. Maintain weight properly in step with the body mass index. Habituate regular exercise and develop a daily pattern of sleep which might help us to scale back the possibility of developing type-II diabetes [21]

### **E. Nutrition Therapy Recommendations.**

Nutrition interventions should emphasize a range of minimally processed nutrient dense foods in appropriate portion sizes as a part of a healthful eating pattern and provide the individual with diabetes with practical tools for day-to-day food plan and behavior change which will be maintained over the long run. There is no standard plan or eating pattern that works universally for all people with diabetes. So as to be effective, nutrition therapy should be individualized for every patient/client supported his or her individual health goals; personal and cultural preferences; health literacy and numeracy; access to healthful choices; and readiness, willingness, and talent to vary. [17, 18, 19, 20] The evidence is powerful that nutrition therapy provided by dietitian nutritionists is effective and essential within the management of diabetes. However, EB nutrition-therapy interventions must be individualized and implemented in collaboration with the adult with diabetes. Personal preferences (e.g., tradition, culture, religion, health beliefs, goals, and economics) must be considered when recommending eating patterns. Furthermore, outcomes must be monitored and evaluated to see if treatment goals are being met or if a change in overall therapy (medication) is required. The challenge is how best to coach the HCT and persons with diabetes to implement EB diabetes nutrition-therapy interventions into clinical practice and for the self-management of diabetes. A significant challenge for HCTs and educators is that the acceptance, integration, and implementation of digital health technology. [6, 20]

### **F. Conclusion.**

Painful DPN could be a disabling condition affecting up to twenty of those with type 1 or type 2 diabetes. The consequences of living with chronic pain are manifest in activities of daily living leading to reduced quality of life. Not surprisingly, this may result in sleep disturbance, anxiety, and depression. Given the severity of the symptoms in many individuals it's unfortunate that at the present the medications recommended for treatment of this condition are only partially effective and don't address the cause of the pain. In order to develop new therapies, peripheral and central the nervous system targets within the system are studied. Peripheral sensitization arises from the direct effects of glycemic damage to the afferent neuron, and multiple mechanisms are described which will be working in concert to come up with primary hyperalgesia. Central sensitization is a smaller amount well studied, due partly to the large complexity and individuality of the human brain and spinal cord. Studies of central system changes in human subjects with painful DPN suggest that there are functional and neurometabolic changes in areas considered to be a part of the pain matrix in humans that would be indicative of central sensitization, but given the metabolic and vascular insults that are typical of diabetes, further work is required to grasp how the peripheral and central neuronal plasticity combines with vascular and metabolic factors to supply painful DPN

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