



# The Risk Factors in Serum of Peripheral Neuropathy Diabetic and Type 2 Diabetes Patients

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## ABSTRACT

**Aims** The study's purpose was to evaluate the serious risk factor for the neuropathy disease in patients with diabetes

**Materials & Methods** This research was done on 120 subjects classified into 40 with DPN T2DM and 40 with T2DM and 40 healthy considered as a control. As the conditions of the Iraqi Ministry of Health to evaluate the thesis clinically, that the number of samples examined should be at least 120 samples. The collection period was from 1 October 2021 to 1 December 2021. All patients and control groups were collected from medical City Al-Imamian, Al-Kadhmiyain-Baghdad-Iraq. Regression analysis was used to investigate potential risky factorize lead for the DPN in T2DM patients.

**Findings** The spread of DPN in Type 2 diabetic patients was 50% of the multiple logistic transformations revealed in diabetic peripheral neuropathy. The mean value of Duration was significant ( $p < 0.05$ ) for DPN compared with T2DM. The mean value of fasting glucose, HbA1c, and hypertension, for DPN participants, were significantly higher than in T2DM and control groups ( $p = 0.0001$ ). The analysis of variance for vitamin B12 and vitamin D was significant ( $p = 0.0001$ ) for DPN it was lower than for T2DM and control. The mean value of lipid profile was non-significant ( $p > 0.05$ ) between the three groups.

**Conclusion** Diabetic peripheral neuropathy had a high risk of a decrease in their vitamin B12 and vitamin D levels. On another hand, patients with T2DM should follow up on their vitamin levels periodically.

**Keywords** Diabetic peripheral neuropathy; Diabetes Mellitus Type 2; Vitamin B 12; Vitamin D; Lipid

## CITATION LINKS

[1] The prevalence by staged severity of ... [2] Diabetic neuropathy: mechanisms ... [3] The diabetic foot as a proxy for ... [4] Prediction of clamp-derived insulin sensitivity from ... [5] International diabetes ... [6] Diabetic foot ulcers and their ... [7] Diabetes and obesity are the main ... [8] Healthcare utilization and costs in ... [9] Psychosocial factors in painful diabetic ... [10] Diabetic neuropathy: a position statement by the American ... [11] The potential of transdermal nitric oxide ... [12] New perspective in diabetic neuropathy ... [13] Cardiac autonomic neuropathy: risk factors ... [14] Global report on ... [15] Diabetic microvascular disease ... [16] Diabetic peripheral neuropathy in people ... [17] Protease inhibitors from marine actinobacteria as ... [18] Thyroid hormones, peripheral white blood ... [19] Prevalence of cobalamin deficiency ... [20] Impact of vitamin D level in diabetic ... [21] Expert committee recommendations ... [22] Estimation of the concentration of low-density ... [23] Correlation of staging and risk factors ... [24] Value of shear wave elastography ... [25] Identification of independent risk factors ... [26] Characteristics of type 2 diabetes mellitus in Egyptian ... [27] Study the role of dyslipidemia in cases ... [28] Assessment of serum high mobility ... [29] Toll-like receptor 4 and tumor necrosis ... [30] Association of metformin use with ... [31] Vitamin B12 deficiency in patients ... [32] A review on vitamin B12 and diabetic ... [33] Association of vitamin D deficiency ... [34] Association of vitamin D level and nerve ... [35] Association of vitamin D3 and its ... [36] Relationship of serum vitamin D levels ... [37] Association between body fat and diabetic ... [38] Inflammatory biomarkers levels in T2DM Emirati ... [39] Fibrinogen function indexes, potential ... [40] Associations of thyroid hormone levels ... [41] Glycaemia status, lipid profile and ... [42] Pro198 Leu 2017 polymorphism in the ... [43] A systematic review and meta-analysis ...

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## Introduction

Neuropathic etiologies are frequent complication of diabetes mellitus, with pathogenesis of diabetic peripheral sensorimotor neuropathy (DPN) being the most common, force increases approximately 50% of diabetics [1, 2]. The DPN is linked to high morbidity and risk of death, owing in comparison towards its, two main patient assessment findings, Diabetes of the foot, skin lesions and nerve anguish [3-5]. Diabetes of the leg ulcers are caused by a complicated interplay of danger variables as well as patience habits, however, sensory impairment in addition to DPN is the most common reason [6]. Diabetes-related low-limb, troubles are costly and impose a significant a financial burden on sick people, possibly leading to catastrophic results which including lower, limb amputees & dying. [3, 4, 6]. It can also have a range of clinical signs and symptoms, as well as various pathophysiologic mechanisms and A quantity of cardio metabolic risk components, like hypertriglyceridemia and low HDL levels, are frequently related to nerve damage in type 2 diabetes mellitus (T2DM) cases [7]. These heartbreaking signs are frequently severe, leading to depression, anxiousness, sleep problems, and a lower standard of living [8, 9]. Sadly, our knowledge of the pathobiology of DPN is still limited. As a result, we lack efficient illnesses derived from different sources in which to treat the situation; instead, the main element of newer system is to manage hazard factors for DPN, as well as to avoid and manage its ramifications [10]. It is critical that the status was detected early and correctly so that indicators to minimize the risk of foot ulcers complications can be instated [11]. DPN symptoms, which may compliment diagnostic evaluation and aid in the earlier diagnosis of DPN in research and patient assessment [12]. The duration of the disease and the level of blood sugar control are among the major contributing factors to the development of nerve impingement in type 2 diabetic patients [13]. Diabetes complications have such a major impact on individuals affected, according to a WHO document [14]. Diabetes is a major public risk to public wellness of the population. In terms of type 2 diabetics, the results of vascular and endothelial dysfunction [15]. Proven that the general neuropathies, prevalence between type 2 diabetic patients (42.2%) however, it is among the most prevalent and serious diabetes common complication DPN in patients with type 2 diabetes is badly controlled due to their own disguised onset, late diagnostic test, and more complicated sources caused by getting older, overweight, high blood sugar, dyslipidemia, and hypertension [16]. The research results in [17] show that the period of diabetes, as well as glycosylated hemoglobin, are cooperated with significant higher risks of DPN in people with diabetes Furthermore [18].

Diabetic neuropathy causes a variety of clinical issues. Neuropathy of the periphery could also be not possible distinguish itfrom pathology as a result of vitamin B12 reduction as well as will cause permanent nerve damage if correction of deficiency is not prompt [19].

Also Vitamin D deficiency involved in the pathology of diabetic neuropathy Inflammation and high blood sugar are present is thought to be, a severe danger of DPN. In an earlier study, they discovered that one hundred percent of lower, leg the neurons are impacted in cases and controls, with primarily affection affecting nervous system [20].

## Materials and Methods

The study also includes 120 subjects from adult men ages ranging from (35-82) years, forty healthy subjects as a normal control, and 80 patients with Diabetic type 2. The patients' population divided into 2 groups: Diabetic type 2 (T2DM; n=40) and diabetic peripheral neuropathy group (DPN; n=40) as it is one of the conditions of the Iraqi Ministry of Health to evaluate the thesis clinically, that the number of samples examined should be at least 120 samples as the samples presence. The study conducted at Chemistry Department collage of science Mustansiriyah University from 1 October 2021 to 1 December 2021. All patients and control were collected from (AL-Imamian Al Kadhmiyain Medical City Baghdad Iraq) both the patient and the control were evaluated using biochemical tests, immunological and biomedical laboratory tests. All subjects were without any noticeable inflammatory anomalies and, tumors, long-term illnesses Patients' baseline characteristics and control data was collected from patient health registers. The following information was gathered (age sex and height, weight; DM duration diabetic foot; smoking status; hypertension; family history). The Identification of Diabetic Peripheral Neuropathy for the DPN patient group Confirmed by previous medical reported from The Specialized Endocrine and Diabetes Center Iraqi ministry of health with positive results from neurologic medical tests and peripheral nerve tests. In addition, a medical evaluation involving review of for each patient and clinical signs and symptoms of psychological examination and in most patients with DPN, recorded (Tingling "pins and needles" or numbness in the hands and feet. Sharp burning severe pain, especially at night. Loss sensitivity to touch. Muscle weakness). Six milliliters of blood taken from fasting patients and control groups blood samples obtained during (8:00-11:00). Each blood sample divided into two parts the first one tow mL of blood was transferred into EDTA-containing tubes for HbA1C measurements. Second, four milliliters were transmitted into gel tubes for measurements of biochemistry and endocrine (glucose and lipid

profile vitamin D and vitamin B12). Allow clotting for 30 minutes, after that, the serum was centrifuged for 10 min at (3000 rpm) divided into Eppendorf, and kept at  $\{-20^{\circ}\text{C}\}$  until the related parameters were measured.

The subjects (body mass index) splitted the research measured data into normal (19-24.9) and overweight (25-29.9) Using the formula:

$$\text{BMI} = \text{Weight (kg)} / \text{Height (m}^2\text{)}^{[21]}$$

Additionally, Glucose Hexokinase (Glu H) and enzymatic hemoglobin A1C (HbA1c) and Vitamin D with vitamin B12 levels and lipid profile (total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) were calculated utilizing an automated clinical chemistry analyzer (Atellica CH 930 Siemens, German), and low-density lipoprotein (LDL) levels were calculated using the Friedewald equation [22].

The statistical impacts of the study were calculated in SPSS 26 software by ANOVA statistical test. Utilized to calculate the quantitative variables for parameter from the data reported that also comprised the mean, standard-deviation (SD), P-values and using an analysis of variance (ANOVA), T test were conducted to determine whether there were significant differences in different variables among all groups data analysis significance was found when the P value  $<0.05$  and highly significant at ( $p < 0.01$ ).

## Findings

The findings were revealed in Table 1. There were significant differences in terms of hypertension, and duration between groups ( $p < 0.05$ ). There was no significant difference between groups in terms of Total cholesterol, Triglyceride, HDL, VLDL, and LDL ( $p > 0.05$ ; Table 2).

**Table 1)** Mean of demographic variables of subjects

Parameter	Control (n=40)	T2DM (n=40)	DPN (n=40)	p-value
Age (years)	50.3000±10.6583	55.1250±10.7541	53.4500±8.0126	0.090
Height (m)	17.75±10.8480	168.025±10.5112	169.375±10.4922	0.519
Weight (kg)	76.1000±12.9016	76.9500±12.2954	76.6000±11.7708	0.953
Smoking	1.6500±.4830	1.5250±0.5057	1.4000±0.4961	0.082
hypertension	1.8500±.3616	1.5500±0.5038	1.3750±0.4902	0.0001
Duration (years)	-	4.2750±4.3263	11.4250±7.0815	0.0001
BMI (kg/m <sup>2</sup> )	26.0315±3.2066	27.1086±2.2426	26.5914±2.2235	0.184

**Table 2)** Mean±SD results of clinical and biochemical characteristics of subjects

Parameter	Control (A)	T2DM (B)	DPN (C)	p-value
Fasting Glucose (mg/dl)	94.9625±9.0301	169.1610±45.5767	283.6900±110.4458	0.0001
Hba1c	5.4260±0.4610	7.6425±1.34517	9.7925±2.10554	0.0001
Vitamin B12 (pg/ml)	403.1500±152.6570	447.7000±127.2028	274.0750±86.3191	0.0001
Vitamin D (ng/ml)	24.9735±10.3793	17.9388±7.7695	12.8885±3.0710	0.0001
Total Cholesterol (mg/dl)	172.5433±38.2513	176.1500±41.6589	187.4250±57.0900	0.330
Triglyceride (mg/dl)	165.9750±104.2626	204.2000±92.2352	218.6250±129.5684	0.090
HDL (mg/dl)	37.2975±8.3415	34.2200±6.2857	37.4325±12.3778	0.225
VLDL (mg/dl)	32.9281±19.6860	40.8375±18.4531	46.2342±35.5965	0.072
LDL (mg/dl)	104.6490±35.6322	107.3512±37.3463	103.0325±46.1045	0.888

Note: High-density lipoprotein: HDL; low density lipoprotein: LDL; very-low-density lipoprotein: VLDL

The result of glucose was shown the average glucose level was a significant increase ( $p < 0.05$ ) among group A and B groups and between group A and C groups as well as intergroup B and C ( $p < 0.05$ ). Fasting glucose levels have been greater in patients, suffering from diabetic peripheral neuropathy as compared, to other, groups. However, the average value, of HbA1c was significant between groups A and B in addition to groups A and C and between B and C. The mean value of HbA1c was the highest intergroup diabetic neuropathy in comparison to others. The Mean value of Vitamin B12 was the lowest intergroup diabetic neuropathy as a comparison to groups B and A the mean value of Vitamin B12 was significant ( $p < 0.05$ ) among groups A and C and as well as ( $p < 0.05$ ) but that was not statistically significant between-group A and B ( $p = 0.16$ ). The mean value of Vitamin D levels had lowered in patients with diabetic peripheral neuropathy especially in comparison to other groups the mean, the value of, Vitamin D was

significant ( $p < 0.05$ ) among groups A and B and significant ( $p < 0.05$ ) among group A and C also intergroup B and C. The average triglyceride level was significant ( $p = 0.049$ ) between groups A and C and non-significant ( $p = 0.086$ ) between groups A and B as well as ( $p = 0.568$ ) in intergroup B and C. The mean value of VLDL was significant ( $p = 0.042$ ) among groups A and C and non-significant ( $p = 0.068$ ) between groups A and B as well as ( $P = 0.398$ ) intergroup B and C. VLDL levels have been significantly larger in diabetic type2 patients as compared to other groups. The remaining parameters of lipid profile (Mean value of total cholesterol was, HDL, LDL) were statistically insignificant between the three groups ( $p > 0.05$ ).

## Discussion

The findings revealed in the Demographic values show non-significant differences in (age, BMI, Height, weight, and current smoking) among participants with T2DM and DPN and the healthy

control, group ( $p > 0.05$ ). This proved that our selection of the subject of the control was right them reducing and eliminating any risk factor that might affect the results and thus agree with other research works [23-25]. Furthermore, this research found that the results of the comparison of the DM duration were significant differences in the DPN group's longer duration compared to the T2DM group ( $p < 0.05$ ) [26].

According to this study's findings, there were significant results indicated in hypertension in the DPN group compared to the T2DM group and control group ( $p = 0.0001$ ) agreeing with a previous study [27].

The results in agreement with other previous studies reported the levels of fasting glucose and HbA1c for diabetic neuropathy patients were significantly higher than in type 2 DM patients and healthy patients [28-30].

The analysis of variance for Vit B12 was significant and the result was in agreement with other previous studies that concluded a significant decrease in vitamin B12 concentrations and possessing a positive diagnosis of diabetic neuropathy [31, 32].

The analysis of Vit D levels in agreement with other previous studies concluded that Vit D is the main deficiency in patients with DPN. The descriptive Statistics for main markers in the diabetic peripheral neuropathic, diabetic type 2 and control groups [33-36]. The lipid profile (TC); (TGs); (HDL); (LDL); (VLDL). They were not associated with the study and this is consistent with previous research that reported the lipid profile was not associated with DPN [37-39].

results data of glucose and HbA1c were shown The average levels were significant both fasting glucose and HbA1c levels have been greater in patients, suffering from diabetic peripheral neuropathy and its agreement with the previous study [28, 29].

The Vit B12 level was lowest in patients with diabetic neuropathy that is because Vit B12 acted, as a neurotrophic factor related to diabetic Peripheral neuropathy vitamin B12 deficiency will cause permanent nerve damage [19].

The Vit D levels are lowered in patients suffering from diabetic neuropathy, especially in comparison to other patients without diabetic neuropathy [33, 34].

Another research analyzes the variables of the blood lipids among patients with and without diabetic peripheral neuropathy and reported that non-significant in VLDL levels among these groups [40]. According to our research, Mohapatra & Damodar reported same results for the comparison of lipid levels and carbohydrate restriction among various stages of diabetic peripheral neuropathy and controls. They reported that a significant increased triglyceride levels in diabetic peripheral neuropathy patients' comparison to controls [41].

However, these results of triglyceride and VLDL were statistically in contrast to our study because of

the different demographic and clinical profiles of studied subjects such as age at study duration of diabetes cardiovascular disease essential hypertension other MV complications family history of diabetes.

The remaining parameters of lipid profile (Mean value of total cholesterol was, HDL, LDL) were statistically insignificant between-group (AvsB) and (BvsC) and (AvsC) ( $p > 0.05$ ) in agreement with previous reported [36, 37]. Lipid profile and its relationship with DPN biologically, changes in lipid levels are obvious characteristics of control patients the Future research is needed to fully understand the relationship between the serum lipid profile and DPN. Because other studies indicated there is a high incidence of dyslipidemia in T2DM patients, and dyslipidemia is linked to Diabetic Peripheral Neuropathy. Quite a lot of pathological modifications in nerve cells, nerve fibers, and vascular endothelial cells, can result in nerve dysfunction and, eventually, death DPN caused by hyperglycemia and dyslipidemia, together with altered insulin signaling [42, 43].

## Conclusion

There is a relationship between peripheral diabetic neuropathy with risk factors and clinical parameters, which had a longer disease duration. The fasting glucose and Hba1c were significant for DPN higher than in T2DM and control groups Therefore, the risk factors considered as independent coloration for DPN diagnosis future studies on (a large scale) should be carried out to confirm these research results.

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