# Analysis of Variance of Diabetic Neuropathic Pain Interference, Intensity and Hypertension Types in Ghana

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**Research Article**

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# Abstract

Diabetic Neuropathic Pain (PDN) is the most prevalent chronic complication of diabetes and affects 30–90% of patients with adjuvant complications. Hypertension has been found to increase the risk of long-term vascular complications of Type 2 diabetes mellitus which includes peripheral sensory diabetic neuropathic pain. However, the relationship between Diabetic Neuropathic Pain Interference, Intensity and Hypertension types among Type 2 Diabetes has not been extensively investigated. This study investigates the relationship between hypertension PDN intensity interference and pain intensity. The research design was a cross-sectional descriptive design. A sample of 125 participants was systematically selected for the study A demographic questionnaire and the Brief Pain Inventory for Painful Diabetic Peripheral Neuropathy was used to collect the data. ANOVA was used to determine whether there is an association, between the hypertension types and PDN pain intensity and interference. The study concluded that there was no relationship between Hypertension types and PDN intensity and interference. The study further discovered that whether a patient had normal hypertension, pre-hypertension, stage 1 hypertension, or Stage 2 hypertension, they felt equal pain.


# Background

Diabetic neuropathies are the most prevalent chronic complications of diabetes and affect 30–90% of patients with adjuvant complications.[1] Painful Diabetic Neuropathy (PDN) is "the presence of symptoms and signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes." It results in muscle weakness and affects movement, primarily in the legs, with the initial symptoms of cramps or weakness in the muscles of the big toe and later in the entire foot. [3, 4, 5]

Hypertension has been proposed as an independent risk factor for diabetic neuropathy. Hypertension has also been found to increase the risk of long-term vascular complications of Type 2 diabetes mellitus (T2DM) which includes peripheral sensory diabetic neuropathic pain and death. [6, 7]

Commonly known as Blood Pressure, hypertension is a measurement of the force of your blood against the blood vessel walls usually denoted by a fraction-like (a/b) figure and measured in millimetres of mercury –mmHg. [6, 8] In hypertension measurement and recording, the top number is the pressure when your heart contracts and pushes blood out (systolic) and the bottom number is the pressure when the heart relaxes between beats (diastolic). Hypertension is defined as blood pressure ≥ 140/90 mmHg, while pre-hypertension refers to systolic blood pressure 120–139 mmHg or diastolic 80–89 mmHg and normal blood pressure is referred to as < 120/80 mmHg. [8, 9, 10, 1, 12, 13, 14] “Hypertension [14] is common among patients with diabetes, with the prevalence depending on type and duration of diabetes, age, sex, race/ethnicity, BMI, history of glycemic control, and the presence of kidney disease, among other factors.” [15, 16, 17]

The main comorbidity of neuropathy is hypertension and knowledge of such comorbidities has the potential to enrich the therapeutic strategy in clinical intervention and management of diabetic

neuropathic pain. [18] However, the relationship between Diabetic Neuropathic Pain Interference, Intensity and hypertension types among Type 2 Diabetes has not been extensively investigated. A study on the prevalence of hypertension and diabetes mellitus (DM) in Ghana stressed the need for further research into the association between PDN characteristics and hypertension. [19]

### Aim:

This study aimed to examine the relationship between hypertension (normal hypertension, pre-hypertension, stage1 hypertension and stage 2 hypertension) and PDN intensity (worst pain, least pain, average pain, and current pain) and PDN interference (general activity, walking, work, mood, enjoyment of life, relations with others, and sleep).

## Method

The research design for this study was a cross-sectional descriptive design. [20, 21] A sample of 125 participants was systematically selected for the study. The inclusion criteria for this phase were: (a) adult patients attending the diabetic clinic of the Komfo Anokye Teaching hospital; (b) patients should have been diagnosed with PDN. These criteria were all met by each participant who was recruited to participate in the study.

Consented participants were asked to complete a demographic questionnaire and BP was assessed in all participants on the non-overriding arm, guaranteeing accurate cu size, with an automated device DINAMAP PRO 400 (Critikon, FL) in the sitting position after 5 minutes' rest on 2 occasions. Hypertension was recorded as maintaining a normal blood pressure (BP) of a systolic BP (SBP) of less than 120 mm Hg and a diastolic BP (DBP) of less than 80 mm Hg as described in the WHO/ISH Guidelines [22, 23].

The Brief Pain Inventory for Painful Diabetic Peripheral Neuropathy (BPI-PDN) was the instrument used in collecting data on pain intensity and interference of respondents. The BPI allowed patients to rate the severity of their pain and the degree to which their pain interfered with common dimensions of feeling and function [23, 24]. The BPI measures two domains — pain intensity (severity) and the impact of pain on functioning (interference) [25]

Double data entry was conducted with validation in Epi data 3.1; and entered into the *Statistical Package for the Social Sciences*, SPSS® (version 22.0). Data was prepared by logging the data, making a codebook, entering the data into the computer, and checking for accuracy to eliminate errors [26]. ANOVA was used to determine whether there is an association, between the comorbidity of hypertension and diabetic neuropathy pain intensity and interference [27].

### Ethics:

Ethical clearance for this study was twofold. The first level of ethical clearance was institutional, where the University of the Western Cape requires that all students' projects be ethically cleared for stringent ethical scrutiny before conducting research. After ethical application, the Biomedical Research Ethics

Committee (BMREC) at the University of the Western Cape ratified and approved this project after all recommended changes were accepted. The second level of clearance was granted by the Research and Development Unit of the Komfo Anokye Teaching Hospital as well as the Committee for Human Research Publications and Ethics of the School of Medical Sciences, Kwame Nkrumah University of Science and Technology.

# Results And Analysis

### Pain Intensity and Hypertension Types:

In an ANOVA, what best described normal hypertension patients' pain at its worst in the last week before the data collection did not significantly differ from that of their pre-hypertension, stage-1 hypertension, and that of their stage-2 hypertension counterparts ($F = 1.240, p = 0.300$). Similarly, what best described normal hypertension patients' pain at its least in the last week before the data collection did not significantly differ from that of their pre-hypertension, stage-1 hypertension, and that of their stage-2 hypertension counterparts ($F = 2.383, p = 0.770$). On what best described their pain on average, it turned out that some of the normal hypertension patients did not significantly differ from that of their pre-hypertension, stage-1 hypertension, and that of their stage-2 hypertension counterparts ( $F = 0.718, p = 0.540$) when it came to differences in pain. Finally, in an ANOVA to determine whether there was a significant difference between how much pain hypertension patients had, at the time of the data collection, and that of their pre-hypertension, stage-1 hypertension, or stage-2 hypertension counterparts, it turned out that there was none ($F = 1.491, p = 0.220$).

Analysis of the extent to which pain had interfered with some selected daily activities of respondents is presented in Table 1.1. A one-way analysis of variance was conducted to evaluate the null hypothesis that there is no difference in the level of interference of pain in participants' general activity based on their BP status ($M = 4.44$, $SD = 3.144$, $N = 117$). The independent variable, BP, referring to the blood pressure status, included four groups: Normal Blood Pressure ($M = 5.67$, $SD = 2.744$, $N = 18$), Pre-Hypertension ($M = 4.25$, $SD = 3.186$, $N = 48$), Stage-1 Hypertension ($M = 4.28$, $SD = 2.999$, $N = 29$) and Stage-2 Hypertension ($M = 4.05$, $SD = 3.498$, $N = 22$).

Table 1.1
ANOVA for Pain Intensity against Blood Pressure Status

| Blood Pressure Status | | What best describes your pain at its worst in the last week | What best describes your pain at its least in the last week | What best describes your pain on the average | How much pain do you have right now? |
|---|---|---|---|---|---|
| Normal Hypertension | N | 17 | 17 | 18 | 17 |
| | Median | 8.00 | 2.00 | 5.00 | 5.00 |
| | Mean | 7.65 | 3.18 | 5.06 | 5.24 |
| | Std. Deviation | 2.262 | 2.744 | 1.830 | 2.538 |
| Pre-hypertension | N | 45 | 48 | 47 | 48 |
| | Median | 7.00 | 2.00 | 5.00 | 3.00 |
| | Mean | 6.16 | 2.44 | 4.11 | 3.56 |
| | Std. Deviation | 3.119 | 2.422 | 2.434 | 2.938 |
| Stage-1 hypertension | N | 29 | 30 | 31 | 31 |
| | Median | 7.00 | 1.50 | 4.00 | 3.00 |
| | Mean | 6.59 | 2.43 | 4.35 | 3.65 |
| | Std. Deviation | 2.472 | 2.909 | 2.229 | 2.847 |
| Stage-2 Hypertension | N | 22 | 21 | 21 | 22 |
| | Median | 6.50 | 2.00 | 4.00 | 4.00 |
| | Mean | 6.41 | 2.76 | 4.29 | 4.23 |
| | Std. Deviation | 2.557 | 2.897 | 2.667 | 3.545 |
| ANOVA | F | 1.240 | 2.383 | 0.718 | 1.491 |
| | df | 3 | 3 | 3 | 3 |
| | P | 0.30 | 0.77 | 0.54 | 0.22 |

**Source: Field Data Collection (Diabetes Centre - KATH, Ghana)**

**Pain Interference and Hypertension Types:**

**Interference of Pain with Participants' general Activity Based on their BP Status**

The assumption of homogeneity of variances was tested and found tenable using Levene's Test, [$F$ (3, 113) = 1.004, $p$ = 0.394] as represented in Table 1.2. The accompanying ANOVA was not significant [$F$ (3, 113 = 1.117, $p$ = 0.345] at a 95% confidence level. Hence there is significant evidence not to reject the null hypothesis and conclude that there was no significant difference in the level of interference of pain in participants' general activity based on their BP status.

Table 1.2
ANOVA for Pain Interference by Stages of Hypertension

| | N | Mean | SD | 95% Confidence | | F(Num., Denom) | P |
|---|---|---|---|---|---|---|---|
| | | | | Lower Bound | Upper Bound | | |
| How pain has interfered with participants' general activity | | | | | | | |
| Normal Blood Pressure | 18 | 5.67 | 2.744 | 4.30 | 7.03 | 1.117 (3,113) | 0.345 |
| Pre-hypertension | 48 | 4.25 | 3.186 | 3.32 | 5.18 | | |
| Stage-1 hypertension | 29 | 4.28 | 2.999 | 3.14 | 5.42 | | |
| Stage-2 hypertension | 22 | 4.05 | 3.498 | 2.49 | 5.60 | | |
| Total | 117 | 4.44 | 3.144 | 3.86 | 5.01 | | |
| How pain has interfered with participants' mood | | | | | | | |
| Normal Blood Pressure | 18 | 5.33 | 2.808 | 3.94 | 6.73 | 1.482 (3,113) | 0.223 |
| Pre-hypertension | 48 | 3.63 | 2.893 | 2.79 | 4.46 | | |
| Stage-1 hypertension | 29 | 4.17 | 2.953 | 3.05 | 5.30 | | |
| Stage-2 hypertension | 22 | 4.36 | 3.317 | 2.89 | 5.83 | | |
| Total | 117 | 4.16 | 2.997 | 3.61 | 4.71 | | |
| How pain has interfered with participants' walking ability | | | | | | | |
| Normal Blood Pressure | 18 | 5.50 | 2.834 | 4.09 | 6.91 | 1.126 (3,112) | 0.342 |
| Pre-hypertension | 48 | 4.02 | 3.084 | 3.13 | 4.92 | | |
| Stage-1 hypertension | 29 | 4.72 | 3.172 | 3.52 | 5.93 | | |
| Stage-2 hypertension | 21 | 4.95 | 3.552 | 3.33 | 6.57 | | |
| Total | 116 | 4.59 | 3.165 | 4.01 | 5.18 | | |
| How pain has interfered with participants' normal work | | | | | | | |

**Source: Field Data Collection (Diabetes Centre - KATH, Ghana)**

| | N | Mean | SD | 95% Confidence | | F(Num., Denom) | P |
|---|---|---|---|---|---|---|---|
| | | | | Lower Bound | Upper Bound | | |
| Normal Blood Pressure | 18 | 4.61 | 2.638 | 3.30 | 5.92 | 1.034 (3,112) | 0.38 |
| Pre-hypertension | 48 | 3.25 | 2.928 | 2.40 | 4.10 | | |
| Stage-1 hypertension | 29 | 3.97 | 3.168 | 2.76 | 5.17 | | |
| Stage-2 hypertension | 21 | 4.10 | 3.491 | 2.51 | 5.68 | | |
| Total | 116 | 3.79 | 3.057 | 3.23 | 4.36 | | |
| How pain has interfered with participants' relations with other people | | | | | | | |
| Normal Blood Pressure | 17.00 | 2.35 | 2.21 | 1.22 | 3.49 | 0.316 (3,112) | 0.814 |
| Pre-hypertension | 48.00 | 2.44 | 3.09 | 1.54 | 3.34 | | |
| Stage-1 hypertension | 30.00 | 2.97 | 3.54 | 1.65 | 4.29 | | |
| Stage-2 hypertension | 21.00 | 3.05 | 3.77 | 1.33 | 4.77 | | |
| Total | 116.00 | 3.05 | 3.21 | 2.08 | 3.26 | | |
| How pain has interfered with participants' sleep | | | | | | | |
| Normal Blood Pressure | 17.00 | 3.76 | 3.25 | 2.09 | 5.44 | 0.940 (3,113) | 0.424 |
| Pre-hypertension | 48.00 | 3.33 | 3.06 | 2.45 | 4.22 | | |
| Stage-1 hypertension | 30.00 | 4.20 | 3.13 | 3.03 | 5.37 | | |
| Stage-2 hypertension | 22.00 | 4.59 | 3.50 | 3.04 | 6.14 | | |
| Total | 117.00 | 3.85 | 3.19 | 3.27 | 4.44 | | |
| How pain has interfered with participants' enjoyment of life | | | | | | | |
| Normal Blood Pressure | 17.00 | 4.47 | 2.55 | 3.16 | 5.78 | 0.398 (3,112) | 0.754 |
| Pre-hypertension | 48.00 | 3.62 | 2.75 | 2.81 | 4.43 | | |

**Source: Field Data Collection (Diabetes Centre - KATH, Ghana)**

| | N | Mean | SD | 95% Confidence | | F(Num., Denom) | P |
|---|---|---|---|---|---|---|---|
| | | | | Lower Bound | Upper Bound | | |
| Stage-1 hypertension | 30.00 | 3.90 | 2.93 | 2.81 | 4.99 | | |
| Stage-2 hypertension | 21.00 | 4.05 | 3.18 | 2.63 | 5.46 | | |
| Total | 116.00 | 3.90 | 2.84 | 3.38 | 4.42 | | |
| **Source: Field Data Collection (Diabetes Centre - KATH, Ghana)** | | | | | | | |

**Interference of Pain with Participants' Mood Based on their BP Status**

Further, this study performed a one-way analysis of variance to evaluate the null hypothesis that there was no difference in the level of interference of pain in participants' mood based on their BP status ($M$ = 4.16, $SD$ = 2.997, $N$ = 117) as represented in Table 1.2. Here also independent variable, BP, referring to the blood pressure status, had four groups: Normal Blood Pressure ($M$ = 5.33, $SD$ = 2.808, $N$ = 18), Pre-Hypertension ($M$ = 3.63, $SD$ = 2.893, $N$ = 48), Stage-1 Hypertension ($M$ = 4.17, $SD$ = 2.953, $N$ = 29) and Stage-2 Hypertension ($M$ = 4.36, $SD$ = 3.317, $N$ = 22).

The assumption of homogeneity of variances was again tested for this group and found tenable using Levene's Test, [$F$ (3, 113) = 0.383, $p$ = 0.766]. The accompanying ANOVA was not significant [$F$ (3, 113) = 1.482, $p$ = 0.223] at a 95% confidence level. Hence there was significant evidence not to reject the null hypothesis. We, therefore, concluded that there was no significant difference in the level of interference of pain in participants' moods based on their BP status.

**Interference of Pain with Participants' Walking Ability Based on their BP Status**

Again, an analysis of the extent to which pain had interfered with respondents' walking ability is presented in Table 1.2. A one-way ANOVA was conducted to evaluate the null hypothesis that there was no difference in the level of interference of pain in participants' walking ability based on their BP status ($M$ = 4.59, $SD$ = 3.165, $N$ = 116). Here also the independent variable, BP, referring to the blood pressure status, included four groups: Normal Blood Pressure ($M$ = 5.50, $SD$ = 2.834, $N$ = 18), Pre-Hypertension ($M$ = 4.02, $SD$ = 3.084, $N$ = 48), Stage-1 Hypertension ($M$ = 4.72, $SD$ = 3.172, $N$ = 29) and Stage-2 Hypertension ($M$ = 4.95, $SD$ = 3.556, $N$ = 21).

The assumption of homogeneity of variances was again tested for this group and found tenable using Levene's Test, [$F$ (3, 112) = 1.038, $p$ = 0.379]. The accompanying ANOVA was not significant [$F$ (3, 112) = 1.034, $p$ = 0.380] at a 95% confidence level. This, therefore, implied that there was significant evidence not to reject the null hypothesis and concluded that there was no significant difference in the level of interference of pain in participants' walking ability based on their BP status.

### Interference of Pain with Participants' Normal Work Based on their BP Status

Furthermore, an analysis of the extent to which pain had interfered with respondents' normal work is presented in Table 1.2. A one-way ANOVA was conducted to evaluate the null hypothesis that there was no difference in the level of interference of pain in participants' normal work based on their BP status ($M$ = 3.79, $SD$ = 3.057, $N$ = 116). Once again, the independent variable, BP, referring to the blood pressure status, included four groups: Normal Blood Pressure ($M$ = 4.61, $SD$ = 2.638, $N$ = 18), Pre-Hypertension ($M$ = 3.25, $SD$ = 2.928, $N$ = 48), Stage-1 Hypertension ($M$ = 3.97, $SD$ = 3.168, $N$ = 29) and Stage-2 Hypertension ($M$ = 4.10, $SD$ = 3.491, $N$ = 21).

For the inferential part of the computation, the assumption of homogeneity of variances was tested and found tenable using Levene's Test, [$F$ (3, 112) = 1.695, $p$ = 0.172]. The accompanying ANOVA was not significant [$F$ (3, 112) = 1.034, $p$ = 0.380] at a 95% confidence level. There was therefore significant evidence not to reject the null hypothesis and concluded that there was no statistically significant difference in the level of interference of pain in participants' normal work based on their BP status.

### Interference of Pain with Participants' Relations with Other People Based on their BP Status

We present an analysis of the extent to which pain interfered with respondents' relations with other people (Table 1.2). To ascertain that, a one-way analysis of variance was conducted to evaluate the null hypothesis that there was no difference in the level of interference of pain in participants' relations with other people based on their BP status ($M$ = 2.67, $SD$ = 3.21, $N$ = 116). Once again, the independent variable, BP, referring to the blood pressure status, included four groups: Normal Blood Pressure ($M$ = 2.35, $SD$ = 2.21, $N$ = 17), Pre-Hypertension ($M$ = 2.44, $SD$ = 3.09, $N$ = 48), Stage-1 Hypertension ($M$ = 2.97, $SD$ = 3.54, $N$ = 30) and Stage-2 Hypertension ($M$ = 3.05, $SD$ = 3.77, $N$ = 21).

For this computation as well, the assumption of homogeneity of variances was tested and, this time was not found tenable using Levene's Test, [$F$ (3, 112) = 5.556, $p$ = 0.001]. Therefore, rather than going ahead with the use of ANOVA to ascertain the evidence of any effect of pain on respondents' relations with other people based on their BP status, we used the robust test of equality of means, which is the Brown-Forsythe [$F$ (3, 82) = 0.324, $p$ = 0.808] at 95% confidence level. There was significant evidence not to reject the null hypothesis and concluded that there was no significant difference in the level of interference of pain in participants' relations with other people, based on their BP status.

### Interference of Pain with Participants' Sleep Based on their BP Status

We further present an analysis of the extent to which pain had interfered with respondents' sleep in Table 1.2. A one-way analysis of variance was conducted to evaluate the null hypothesis that there was no difference in the level of interference of pain in participants' sleep based on their BP status ($M$ = 3.85, $SD$ = 3.190, $N$ = 117). As usual, the independent variable, BP, referring to the blood pressure status, included four groups: Normal Blood Pressure ($M$ = 3.76, $SD$ = 3.25, $N$ = 17), Pre-Hypertension ($M$ = 3.33, $SD$ = 3.06, $N$ = 48), Stage-1 Hypertension ($M$ = 4.20, $SD$ = 3013, $N$ = 30) and Stage-2 Hypertension ($M$ = 4.59, $SD$ = 3.50, $N$ = 22).

Once again, the assumption of homogeneity of variances was tested and found tenable using Levene's Test, [$F$ (3, 113) = 0.639, $p$ = 0.591]. The accompanying ANOVA was not significant [$F$ (3, 113) = 0.940, $p$ = 0.424] at a 95% confidence level. Hence there was again significant evidence not to reject the null hypothesis and concluded that there was no significant difference in the level of interference of pain in participants' sleep based on their BP status.

### Interference of Pain with Participants' Enjoyment of Life Based on their BP Status

Finally, we performed an analysis of the extent to which pain had interfered with participants' enjoyment of life (Table 1.2). To achieve this, a one-way analysis of variance was as usual conducted to evaluate the null hypothesis that there was no difference in the level of interference of pain in participants' enjoyment of life based on their BP status ($M$ = 3.90, $SD$ = 2.84, $N$ = 116). Here too, the independent variable, BP, referring to their blood pressure status, included four groups: Normal Blood Pressure ($M$ = 4.47, $SD$ = 2.55, $N$ = 17), Pre-Hypertension ($M$ = 3.62, $SD$ = 2.75, $N$ = 47), Stage-1 Hypertension ($M$ = 3.90, $SD$ = 2.93, $N$ = 30) and Stage-2 Hypertension ($M$ = 4.05, $SD$ = 3.180, $N$ = 22).

Once again, the assumption of homogeneity of variances was tested and found tenable using Levene's Test, [$F$ (3, 112) = 1.110, $p$ = 0.348]. The accompanying ANOVA was also not significant [$F$ (3, 112) = 0.398, $p$ = 0.754] at a 95% confidence level. Hence there was significant evidence not to reject the null hypothesis and concluded that there was no significant difference in the level of interference of pain in participants' enjoyment of life based on their BP status.

In summary, therefore, there was no statistically significant difference in the level of interference of pain in participants' general activity, their mood, their walking ability, their normal work, their relations with people, their sleep, and their enjoyment of life-based on their BP status in this study. In other words, irrespective of their BP status, the pain did not have any form of interference with their general activity in life, their mood, their walking ability, their normal work, their relations with people, their sleep, and their enjoyment of life.

## Discussion

Previous studies link neuropathic pain with interference with daily activities [28, 29]. Others relate neuropathic pain with a disability, quality of life and psychosocial impairment [30, 31]. Other studies, however, have indicated that pain may be associated with poor quality of life [32] while others also have reported that symptoms of pain may be associated with reduced well-being or quality of life [33]. However, this study suggested that there was no relationship between hypertension and pain intensity. There was also no relationship between hypertension types PDN intensity and interference, per this study.

The study rated pain intensity as worst pain, least pain, average pain, all in the past one week and current pain as the four pain levels. These were each a separate variable on which each respondent or patient was assessed. Each level was self-determined by each of the patients on a pain intensity scale between 0 (meaning no pain at all) and 10 (meaning the highest pain). Hypertension, an ordinal variable in the

study, was also recoded into four levels, being normal hypertension, pre-hypertension, stage1 hypertension and Stage2 hypertension. The study discovered that whether a patient had normal hypertension, pre-hypertension, stage1 hypertension or Stage2 hypertension, they felt equal pain, whether worst pain in the past one week, least pain in the past one-week, average pain in the past one week or current pain. This, therefore, meant that pain was not a determinant of hypertension or the intensity of hypertension among PDN patients, which was contrary to numerous studies, which have associated hypertension with PDN [34, 35, 36, 37, 38, 39]. Other studies also suggested that hypertension could influence the development of PDN [40]. From the above, the results of existing studies indicate that the association between hypertension and pain is bidirectional. While some authors would have it that pain leads to hypertension [41, 42] others also suggest that hypertension may lead to pain [43, 44, 45]. It is, however, obvious that there is the need to ascertain the relationships or associations between the causal factors and hypertension so that durable solutions may be identified. Hence the varieties or variations in findings are very much welcomed.

# Conclusion

Regarding the relationship between hypertension, PDN intensity and PDN Interference, this study found that there was no relationship between Hypertension types and pain intensity on one side. There was also no relationship between hypertension and PDN interference. The study further discovered that whether a patient had normal hypertension, pre-hypertension, stage 1 hypertension or Stage 2 hypertension, there was no significant difference in the pain felt, whether worst pain in the past one week, least pain in the past one-week, average pain in the past one week or current pain. Furthermore, there was no association between hypertension types (normal hypertension, pre-hypertension, stage 1 hypertension, or Stage 2 hypertension) and PDN interference (general activity, walking, work, mood, enjoyment of life, relations with others, and sleep). This, therefore, implied that pain was not a determinant of hypertension or the intensity or interference of pain a determinant of hypertension among PDN patients.

# Declarations

- **ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

For this study, the Research and Development Unit of the Komfo Anokye Teaching Hospital and the Research and Ethics Committee of the School of Medical Sciences, Kwame Nkrumah University of Science and Technology granted ethical clearance

Respondents were required to sign an informed consent form prior to participation as evidence of their agreement to participate in the study as well as of their full understanding of the research procedures.

- **CONSENT FOR PUBLICATION**

Respondents were required to sign a consent form for publication prior to participation as evidence of their agreement to publish the findings of this study.

- **AVAILABILITY OF DATA AND MATERIALS**

All of the documents (inventories and scales) were secured in a cupboard in a locked office of the lead author. The acceptable guideline is that research records need to be retained for a minimum of five years; however, if research records are kept in a secure location, they may be kept indefinitely.

- **COMPETING INTERESTS**

They’re no competing interest


- **FUNDING**

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- Authors' contributions - provide individual author contribution
- Adzika A. Vincent (Lead author and conceptualization)
- John Appiah Poku (Supervising author and methodology)
- David Mensah (Statistician and Data Analysis
- Athena Pedro (Literature review and editing)
- Collins S. Ahorlu (Literature review and final editing)
- Safo Kantanka (Field work and data collection)
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# References

1. Callaghan, B. C., Little, A. A., Feldman, E. L., & Hughes, R. A. (2012). Enhanced glucose control for preventing and treating diabetic neuropathy. Cochrane Database Syst Rev, *6*(6), CD007543. https://doi.org/10.1002/14651858.cd007543.pub2
2. Kaur, S., Pandhi, P., & Dutta, P. (2011). Painful diabetic neuropathy: an update. Annals of neurosciences, *18*(4), 168–175. https://doi.org/10.5214/ans.0972-7531.1118409
3. Dyck, P. J., Albers, J. W., Andersen, H., Arezzo, J. C., Biessels, G. J., Bril, V., Feldman, E. L., Litchy, W. J., O'Brien, P. C., Russell, J. W., & Toronto Expert Panel on Diabetic Neuropathy. (2011). Diabetic polyneuropathies: update on research definition, diagnostic criteria and estimation of severity. Diabetes Metab Res Rev, *27*(7), 620–628. https://doi.org/10.1002/dmrr.1226
4. Malik, R. A., Veves, A., Tesfaye, S., Smith, G., Cameron, N., Zochodne, D., Lauria, G., & Toronto Consensus Panel on Diabetic Neuropathy. (2011). Small fibre neuropathy: Role in the diagnosis of diabetic sensorimotor polyneuropathy. Diabetes Metab Res Rev, *27*(7), 678–684. https://doi.org/10.1002/dmrr.1222
5. Pop-Busui, R., Boulton, A. J. M., Feldman, E. L., Bril, V., Freeman, R., Malik, R. A., Sosenko, J. M., & Ziegler, D. (2017). Diabetic neuropathy: A position statement by the American Diabetes Association. Diabetes Care, *40*(1), 136–154. https://doi.org/10.2337/dc16-2042
6. Chawla, A., Chawla, R., & Jaggi, S. (2016). Microvascular and macrovascular complications in diabetes mellitus: Distinct or continuum?. Indian journal of endocrinology and metabolism, *20*(4), 546–551. https://doi.org/10.4103/2230-8210.183480
7. Ansari, P.; Hannan, J.M.A.; Azam, S.; Jakaria, M. (2021) Challenges in Diabetic Micro-Complication Management: Focus on Diabetic Neuropathy. Int. J. Transl. Med. 2021, 1, 175–186. https://doi.org/10.3390/ijtm1030013
8. Vinik AI, Pittenger GL, McNitt P, Stansberry KB. Diabetic neuropathies: an overview of clinical aspects, pathogenesis, and treatment. In: LeRoith D, Taylor SI, Olefsky JM, eds. *Diabetes Mellitus: A Fundamental and Clinical Text* 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003:911–934.
9. Singh, S., Shankar, R., & Singh, G. P. (2017). Prevalence and Associated Risk Factors of Hypertension: A Cross-Sectional Study in Urban Varanasi. *International journal of hypertension*, *2017*, 5491838. https://doi.org/10.1155/2017/5491838
10. Chobanian A. V., Bakris G. L., Black H. R., et al. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension. 2003;42(6):1206–1252. DOI: 10.1161/01.HYP.0000107251.49515.c2.
11. Reboussin, D. M., Allen, N. B., Griswold, M. E., Guallar, E., Hong, Y., Lackland, D. T., Miller, E., 3rd, Polonsky, T., Thompson-Paul, A. M., & Vupputuri, S. (2018). Systematic Review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.

Journal of the American College of Cardiology, *71*(19), 2176–2198. https://doi.org/10.1016/j.jacc.2017.11.004

12. Shimamoto K, Ando K, Fujita T, Hasebe N, Higaki J, Horiuchi M, et al. The Japanese Society of Hypertension Guidelines for the management of hypertension (JSH 2014). Hypertens Res 2014; 37: 253–390.
13. Lee CJ, Hwang J, Lee YH, Oh J, Lee SH, Kang SM, et al. Blood pressure level associated with a lowest cardiovascular event in hypertensive diabetic patients. J Hypertens 2018; 36: 2434–2443
14. De Boer I.H., Bangalore S., Benetos A. Diabetes and hypertension: a position statement by the American Diabetes Association. Diabetes Care. 2017;40(9):1273–1284. [PubMed]
15. Al-Azzam, N., Al-Azzam, S., Elsalem, L., & Karasneh, R. (2020). Hypertension prevalence and associated factors among patients with diabetes: A retrospective cross-sectional study from Jordan. Annals of medicine and surgery (2012), *61*, 126–131. https://doi.org/10.1016/j.amsu.2020.12.038
16. Akalu, Y., & Belsti, Y. (2020). Hypertension and Its Associated Factors Among Type 2 Diabetes Mellitus Patients at Debre Tabor General Hospital, Northwest Ethiopia. Diabetes, metabolic syndrome and obesity: targets and therapy, *13*, 1621–1631. https://doi.org/10.2147/DMSO.S254537
17. de Boer IH, Bakris G, Cannon CP. Individualizing Blood Pressure Targets for People With Diabetes and Hypertension: Comparing the ADA and the ACC/AHA Recommendations. JAMA. 2018 Apr 3;319(13):1319–1320. DOI: 10.1001/jama.2018.0642. PMID: 29543954.
18. Papanas, N., & Ziegler, D. (2015). Risk Factors and Comorbidities in Diabetic Neuropathy: An Update 2015. The review of diabetic studies: RDS, *12*(1–2), 48–62. https://doi.org/10.1900/RDS.2015.12.48
19. Cook-Huynh M, Ansong D, Steckelberg RC, Boakye I, Seligman K, Appiah L, Kumar N, Amuasi JH. Prevalence of hypertension and diabetes mellitus in adults from a rural community in Ghana. Ethn Dis. 2012 Summer;22(3):347–52. PMID: 22870580.
20. Araoye, M. O. (2003). *Research methodology with statistics*. Nathadex Publishers.
21. Bennett, J., Lubben, F., Hogarth, S., & Campbell, B. (2005). Systematic reviews of research in science education: Rigour or rigidity? International Journal of Science Education, *27*(4), 387–406. https://doi.org/10.1080/0950069042000323719
22. Haanpää M, Attal N, Backonja M, Baron R, Bennett M, Bouhassira D, Cruccu G, Hansson P, Haythornthwaite JA, Iannetti GD, Jensen TS, Kauppila T, Nurmikko TJ, Rice AS, Rowbotham M, Serra J, Sommer C, Smith BH, Treede RD. NeuPSIG guidelines on neuropathic pain assessment. Pain 2011; 152:14–27.
23. Ponirakis G, Petropoulos IN, Alam U, Ferdousi M, Asghar O, Marshall A, Azmi S, Jeziorska M, Mahfoud ZR, Boulton AJM, Efron N, Nukada H, Malik RA. Hypertension Contributes to Neuropathy in Patients With Type 1 Diabetes. Am J Hypertens. 2019 Jul 17;32(8):796–803. doi: 10.1093/ajh/hpz058. PMID: 31013342; PMCID: PMC6636691.
24. Cleeland, C. S. (2002). Pain assessment: The advantages of using pain scales in lysosomal storage diseases. Acta Paediatr Suppl, *91*(439), 43–47. https://doi.org/10.1111/j.1651-2227.2002.tb03109.x

25. Zelman, D. C., Gore, M., Dukes, E., Tai, K. S., & Brandenburg, N. (2005). Validation of a modified version of the brief pain inventory for painful diabetic peripheral neuropathy. J Pain Symptom Manage, 29(4), 401–410.
26. Turk, D. C., Dworkin, R. H., Allen, R. R., Bellamy, N., Brandenburg, N., Carr, D. B., Cleeland, C., Dionne, R., Farrar, J. T., Galer, B. S., Hewitt, D. J., Jadad, A. R., Katz, N. P., Kramer, L. D., Manning, D. C., McCormick, C. G., McDermott, M. P., McGrath, P., Quessy, S., … Witter, J. (2003). Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain*, *106*(3), 337–345. https://doi.org/10.1016/j.pain.2003.08.001
27. Trochim, W., Donnelly, J., & Arora, K. (2016). *Research methods: The essential knowledge base* (2nd ed.). Cengage.
28. Vileikyte, L., Leventhal, H., Gonzalez, J. S., Peyrot, M., Rubin, R. R., Ulbrecht, J. S.,Boulton, A. J. (2005). Diabetic peripheral neuropathy and depressive symptoms: The association revisited. Diabetes Care, 28(10), 2378–2383. https://doi.org/28/10/2378
29. Vinik, A., Emir, B., Cheung, R., & Whalen, E. (2013). Relationship between pain relief and improvements in patient function/quality of life in patients with painful diabetic peripheral neuropathy or postherpetic neuralgia treated with pregabalin. Clinical Therapeutics, 35(5), 612–623. https://doi.org/10.1016/j.clinthera.2013.03.008
30. Gylfadottir, Sandra Sif Christensen, Diana Hedevang; Nicolaisen, Sia Kromann; Andersen, Henning; Callaghan, Brian Christopher; Itani, Mustaph; Khan, Karolina Snopek; Kristensen, Alexander Gramm; Nielsen, Jens Steen; Sindrup, Søren Hein; Andersen, Niels Trolle; Jensen, Troels Staehelin; Thomsen, Reimar Wernich; Finnerup, Nanna Brix, Diabetic polyneuropathy and pain, prevalence, and patient characteristics: a cross-sectional questionnaire study of 5,514 patients with recently diagnosed type 2 diabetes, PAIN: March 2020 - Volume 161 - Issue 3 - p 574–583 DOI: 10.1097/j.pain.0000000000001744
31. D. Ziegler, S. Tesfaye, V. Spallone, I. Gurieva, J. Al Kaabi, B. Makovsky, E. Martinka, G. Radulian, K. Thy Nguyen, A.O. Stirban, T. Tankova, T. Varkonyi, R. Freeman, P. Kempler, A. JM Boulton, Screening, diagnosis and management of diabetic sensorimotor polyneuropathy in clinical practice: International expert consensus recommendations, Diabetes Research and Clinical Practice (2021), DOI: https:// doi.org/10.1016/j.diabres.2021.109063
32. Argoff CE, Cole BE, Fishbain DA, Irving GA. Diabetic peripheral neuropathic pain: clinical and quality-of-life issues. Mayo Clin Proc. 2006 Apr;81(4 Suppl): S3-11. DOI: 10.1016/s0025-6196(11)61474-2. PMID: 16608048.
33. Massey, C. N., Feig, E. H., Duque-Serrano, L., Wexler, D., Moskowitz, J. T., & Huffman, J. C. (2019). Well-being interventions for individuals with diabetes: A systematic review. Diabetes research and clinical practice, *147*, 118–133. https://doi.org/10.1016/j.diabres.2018.11.014
34. Bruehl S, Chung OY, Jirjis JN, Biridepalli S. Prevalence of clinical hypertension in patients with chronic pain compared to nonpain general medical patients. Clin J Pain. 2005 Mar-Apr;21(2):147 – 53. doi: 10.1097/00002508-200503000-00006. PMID: 15722808.

35. Tesfaye S, Chaturvedi N, Eaton SE, Ward JD, Manes C, Ionescu-Tirgoviste C, Witte DR, Fuller JH; EURODIAB Prospective Complications Study Group. Vascular risk factors and diabetic neuropathy. N Engl J Med. 2005 Jan 27;352(4):341 – 50. doi: 10.1056/NEJMoa032782. PMID: 15673800.
36. Georgios Ponirakis, Ioannis N Petropoulos, Uazman Alam, Maryam Ferdousi, Omar Asghar, Andrew Marshall, Shazli Azmi, Maria Jeziorska, Ziyad R Mahfoud, Andrew J M Boulton, Nathan Efron, Hitoshi Nukada, Rayaz A Malik, Hypertension Contributes to Neuropathy in Patients With Type 1 Diabetes, American Journal of Hypertension, Volume 32, Issue 8, August 2019, Pages 796–803, https://doi.org/10.1093/ajh/hpz058
37. Krein SL, Hofer TP, Holleman R, Piette JD, Klamerus ML, Kerr EA. More than a pain in the neck: how discussing chronic pain affects hypertension medication intensification. J Gen Intern Med. 2009;24(8):911–916. doi:10.1007/s11606-009-1020-y
38. Sanada, L.S., Tavares, M.R., Sato, K.L. *et al.* Association of chronic diabetes and hypertension in sural nerve morphometry: an experimental study. Diabetol Metab Syndr **7**, 9 (2015). https://doi.org/10.1186/s13098-015-0005-8
39. Gregory JA, Jolivalt CG, Goor J, Mizisin AP, Calcutt NA. Hypertension-induced peripheral neuropathy and the combined effects of hypertension and diabetes on nerve structure and function in rats. Acta Neuropathol. 2012 Oct;124(4):561–73. DOI: 10.1007/s00401-012-1012-6. Epub 2012 Jul 13. PMID: 22791295.
40. Balogun, W. O., & Salako, B. L. (2011). Co-occurrence of diabetes and hypertension: pattern and factors associated with an order of diagnosis among Nigerians. Annals of Ibadan postgraduate medicine, *9*(2), 89–93.
41. Saccò, Marcella & Meschi, Michele & Regolisti, Giuseppe & Detrenis, Simona & Bianchi, Laura & Bertorelli, Marcello & Pioli, Sarah & Magnano, Andrea & Spagnoli, Francesca & Giuri, Pasquale & Fiaccadori, Enrico & Caiazza, Alberto. (2013). The Relationship Between Blood Pressure and Pain. Journal of clinical hypertension (Greenwich, Conn.). 15. 600-5. 10.1111/jch.12145.
42. Giummarra, M. J., Tardif, H., Blanchard, M., Tonkin, A., & Arnold, C. A. (2020). Hypertension prevalence in patients attending tertiary pain management services, a registry-based Australian cohort study. PloS one, *15*(1), e0228173. https://doi.org/10.1371/journal.pone.0228173
43. Forrest KY, Maser RE, Pambianco G, Becker DJ, Orchard TJ. Hypertension as a risk factor for diabetic neuropathy: a prospective study. Diabetes
44. Giummarra, M. J., Tardif, H., Blanchard, M., Tonkin, A., & Arnold, C. A. (2020). Hypertension prevalence in patients attending tertiary pain management services, a registry-based Australian cohort study. PloS one, *15*(1), e0228173. https://doi.org/10.1371/journal.pone.0228173
45. Bruehl S, Chung OY, Jirjis JN, Biridepalli S. Prevalence of clinicalhypertension in chronic pain patients compared to non-pain generalmedical patients.Clin J Pain.2005;21:147–153
46. Georgios Ponirakis, Ioannis N Petropoulos, Uazman Alam, Maryam Ferdousi, Omar Asghar, Andrew Marshall, Shazli Azmi, Maria Jeziorska, Ziyad R Mahfoud, Andrew J M Boulton, Nathan Efron,

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