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Article

Prevalence of Peripheral Neuropathy and Association Between Cardiovascular Disease and Adult Non-Diabetic Peripheral Neuropathy in Trinidad

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Abstract: Introduction: Peripheral neuropathy (PN) is a disease of the peripheral nerves that is insidious in onset, sometimes difficult to diagnose in the early stages and associated with significant morbidity and mortality. The association between diabetic peripheral neuropathy (DPN) and the development of cardiovascular disease (CVD) is well established. However, there are no published studies that have examined the prevalence of non-diabetic PN and its association with the development of CVD in Trinidad and Tobago and the Caribbean. **Methods:** Applying the socioecological model as the theoretical framework, the purpose of this cross-sectional study was to determine the prevalence of non-diabetic PN and to determine whether non-diabetic PN was associated with the development of CVD, participants' income, smoking, alcohol consumption, age, gender, and ethnicity, among an adult population not suffering from diabetes in the South-western part of Trinidad. Primary data from eight general medical practices were analyzed using binary logistic regression in SPSS. **Results:** The prevalence of non-diabetic PN was 21.5%, while in adults with diabetes, the prevalence was 38.1%. CVD was significantly associated with non-diabetic PN (Odds Ratio [OR], 5.47, $p < 0.05$, 95% CI: 1.61 – 18.60). Controlling for the other variables, older adults had a significantly increased risk for developing non-diabetic PN (OR, 2.70, $p < 0.05$, 95% CI: 1.36 – 5.34). Participants' income, smoking status, alcohol consumption, gender, and ethnicity, were not associated with the development of non-diabetic PN. **Discussion:** Non-diabetic PN is insidious in onset and can be difficult to diagnose in the early stages. Patients with CVD, particularly older patients who do not suffer from diabetes, should be aggressively screened for PN. If PN is suspected or diagnosed among these patients, they should be properly managed, as PN is associated with significant mortality and morbidity.

Keywords: peripheral neuropathy; non-diabetic; prevalence; adult; cardiovascular disease; Trinidad

Introduction

PN, a neurologic problem encountered by family physicians and other healthcare providers, is quite common globally [4]. PN has an estimated global incidence of about 77/100,000 inhabitants per year and a prevalence of up to 30% in older people [12]. The overall prevalence of PN in adults with diabetes in the United States is 13.5%, whereas the prevalence in adults without diabetes in the United States is 11.6% [10]. Furthermore, PN is significantly associated with all-cause or overall mortality (hazard ratio [HR]= 1.49; CI, [-1.15, 1.94], $p < 0.001$) [10]. In Latin America and the Caribbean (LAC), diabetic peripheral neuropathy (DPN) is the most prevalent complication of diabetes mellitus and the prevalence of DPN in LAC was 46.5% [17]. Considering that PN is associated with significant morbidity and mortality [13], from a public health perspective, clearly this is a public health burden.

Globally, CVD is a major cause of morbidity and mortality [15]. In Trinidad and Tobago, CVD accounts for approximately 33% of all annual mortality [15]. While DPN, a complication of diabetes is more prevalent in the CVD group [3], little is known about the association between non-diabetic PN and CVD. DPN in patients with CVD has been extensively studied in Trinidad and Tobago and the Caribbean. In other Caribbean countries, over 33% of people who had been diagnosed with diabetes in Barbados, had evidence of PN with a loss of protective sensation [1]. However, there are no published studies that have examined the association between non-diabetic PN and CVD in Trinidad and Tobago. Poverty and low income have been associated with poor health outcomes [14]. It is also argued that individuals with lower incomes tend to have lower educational achievements and less social capital and live in less affluent neighborhoods; these situations have been shown to contribute to poor health outcomes and the development of chronic diseases such as non-diabetic PN [14]. Alcohol consumption and smoking have been associated with the development of non-diabetic PN [6]. We included these variables in the analysis since they could act as important confounders. The lack of information on the association between non-diabetic PN and the development of CVD was the justification for conducting this cross-sectional research study in the South-Western part of Trinidad, which examined whether or not there was an association between non-diabetic PN among adults not suffering from diabetes and cardiovascular disease, income, smoking, alcohol consumption, age, gender, and ethnicity. As of 2011, the population of South-Western Trinidad was 178,410 [5]; the region is the least densely populated region [5].

The theory of the socioecological model [11] was employed in this study. According to [11], the nature of individuals' interaction with their physical and sociocultural environments can impact health and lead to the development of diseases. People's income can influence their access to healthcare services or influence the choices they make about diet and their lifestyle. All these factors can ultimately affect their health outcomes and influence the development of diseases such as non-diabetic PN. By definition, non-diabetic PN encompasses all conditions, excluding diabetes, that cause damage to the peripheral nervous system (PNS), which may include mechanical, toxic, and metabolic causes [16]. Since non-diabetic PN is heterogeneous in its presentation and has a varied etiology, a systematic approach is critical for its evaluation and management. Non-diabetic PN can be encountered by clinicians and healthcare providers in a multitude of clinical settings [13]. This can range from a patient who presents at the emergency department with Guillain-Barre syndrome, to a patient with a suspected carpal tunnel syndrome needing referral to orthopedic surgery or a patient in the oncology unit who recently developed adverse medication reactions to chemotherapy [13]. Globally, non-diabetic PN has been associated with a wide variety of causes such as connective tissue diseases such as amyloidosis, alcohol use, smoking, infectious diseases such as leprosy, Lyme disease, nutritional deficiencies such as vitamins B6, B12, E, and thiamine deficiencies [8]. In a longitudinal study of women's health, women who had experienced perceived discrimination in midlife had 29% higher odds of developing non-diabetic PN, when compared to women who did not report perceived discrimination [7]. However, the association between CVD and non-diabetic PN in adults not suffering from diabetes has not been studied in Trinidad and Tobago and the Caribbean. It is hoped that the results of this research study would fill the gap in the existing knowledge on the association between CVD and non-diabetic PN among adults not suffering from diabetes in Trinidad and Tobago and the Caribbean.

Methods

Study participants, design, and setting: We conducted a cross-sectional study that involved the analysis of primary data to determine the prevalence of PN and whether or not, CVD, income, smoking, alcohol consumption, age, gender, and ethnicity, were associated with the development of non-diabetic PN in South-Western Trinidad. The study setting was eight private general medical practices spread across the South-Western part of Trinidad. The private medical practices were selected to ensure proper coverage and representation of the South-Western part of Trinidad. The sampling frame was all adults who resided in South-Western Trinidad and who attended any of the

eight private general medical practices during the period of this cross-sectional study. Informed consent was obtained from the participants. All adults who attended any of the eight private general medical practices during the period of the cross-sectional study were included. Participants included also resided in the South-Western part of Trinidad. Participants who did not reside in South-Western Trinidad and declined to participate were excluded. The sample size estimated in this study when the allowable error was 5%, was 314.



Figure 1. Map of the South-Western Trinidad. *Note:* Map of South-Western Trinidad showing the main cities (https://www.triniview.com/gallery/main.php?g2_itemId=172156). In the public domain.

Variables/Sources of Data: The dependent variable in this study was non-diabetic PN, defined as the experience of loss of sensation or numbness, ongoing pain, pricking or tingling sensation, burning pain, painful cold or freezing pain over any part of the body, but mostly over the fingers, arms, forearms, thighs, legs, feet, toes, chest, and back, in a person not suffering from diabetes. The independent variables were cardiovascular disease, income, smoking, alcohol consumption, age, gender, and ethnicity. The source of data was primary data collected with a validated and slightly modified questionnaire. The dependent variable, non-diabetic PN, was a categorical dichotomous variable coded as Yes = 1, and No = 0. The independent variables were coded: cardiovascular disease, Yes = 1, No = 0, income (monthly), TT \$2470 to TT \$9800 = 1, and above TT \$9800 = 2, smoking, Yes = 1, No = 0, alcohol consumption, Yes = 1, No = 0, age, 18-49 = 1, 50-79 = 2, 80 and above = 3, gender, male = 1, female = 2, and ethnicity, Black = 1, East Indians = 2, and Others = 3.

Sample Recruitment: Participants were recruited at each of the eight private general medical practices spread across the South-Western part of Trinidad. The respective physicians/medical directors of each of the eight private general medical practices were met in their offices and the details of the research study were presented to them. With the assistance of the various clerical assistants/secretaries at the private general medical practices, potential participants were identified and the research study explained them, including a detailed description or definition of non-diabetic PN. The participants that voluntarily consented were administered the survey questionnaires.

Data Collection Methods: We employed a convenience sampling at the general medical practices until the study's sample size was attained. Primary data on the variables of interest was

collected from the participants using a slightly modified validated DN4 questionnaire, which contained seventeen questions. The DN4 questionnaire has a high diagnostic accuracy [2]. The data was cleaned and entered in SPSS Version 28 and saved in a password protected laptop only accessible to the researchers.

Ethical Considerations: Ethical approval for this study was granted by the relevant local ethics board in Trinidad. To ensure anonymity and confidentiality, participants were de-identified at data collection by assigning each participant a unique identification number. The data collected was stored in a password-protected laptop. The data will be kept for a minimum of 5 years.

Data Analysis: All analyses were conducted using SPSS software version 28. Descriptive statistics were carried out for the dependent variable (non-diabetic peripheral neuropathy), independent variables (cardiovascular disease, income, smoking, alcohol consumption, age, gender, and ethnicity). Chi-Square test was performed to determine any significant associations between the dependent and independent variables. Bivariate logistic regression was performed to assess the association between each of the independent variables and the dependent variable. Associations were considered significant if $p < 0.05$. Multivariate logistic regression analysis was employed to adjust the effects of confounders and included all the variables (dependent and independent) [9].

Results

Table 1. Prevalence of Diabetic and Non-diabetic PN / Characteristics of Study Participants.

Variables	Total Population Non-diabetic PN (IF 235)		Chi Square (<i>p</i>)	Logistic Regression (Bivariate) OR, <i>p</i> , 95% CI
	Yes (%)	No (%)		
Diabetic PN:	38.1	61.9		
Non-diabetic PN:	21.5	78.5		
CVD	6.8	93.2	12.06 (0.01)	5.42(0.02, 1.91 - 15.38)
Income (\$ TT)			0.83(0.36)	0.74(0.36,0.39 - 1.41)
2470-9800 (USD 364-1,445)	59.1			
Over 9800 (over USD 1,445)	40.9			
Smoking	6.0	94	0.01(0.98)	0.98(0.98, 0.26-3.67)
Alcohol	51.9	48.1	0.22(0.64)	0.86(0.64,0.46- 1.60)
Age			18.47(0.01)	3.63(0.01, 1.94—6.78)
18-49	45.9			
50-79	51.1			3.78(0.01, 1.81—7.89)
80 and over	3			11.76(0.03, 2.32-59.51)
Gender			3.07(0.08)	0.57(0.08,0.31 - 1.07)
Male	36.6			
Female	63.4			
Ethnicity			3.82(0.15)	(0.16)
Black	49.8			
East Indians	24.7			0.44(0.06,0.19-1.04)
Others	25.5			0.69(0.34,0.33 - 1.47)

In the bivariate analysis, only cardiovascular disease and age were significantly associated with the development of non-diabetic PN.

Table 2. Multivariate Logistic Regression.

Variable	OR	Sig. (<i>p</i>)	95% CI.
Cardiovascular disease	5.47	0.01	1.61-18.60
Income	0.59	0.18	0.27- 1.27
Smoking	1.13	0.87	0.27 – 4.80
Alcohol	1.12	0.76	0.55-2.29
Age	2.7	0.01	1.36-5.34
Gender	0.69	0.31	0.33-1.42
Ethnicity		0.31	
Blacks			
East Indians	0.48	0.13	0.18-1.25
Others	0.89	0.8	0.38-2.13

In the multivariate analysis, only cardiovascular disease ($p < 0.05$) and age ($p < 0.05$) were significantly associated with non-diabetic PN.

Results: In this study, the number of non-diabetic participants was 235 and 21.5% of these suffered from non-diabetic PN. Among the non-diabetic participants, only 6.8% had a history of CVD, while 59.1% earned a monthly salary of TT2470-9800 (USD 364 -1,445). 51.1% of the participants were between the ages of 50 to 79 years, while females constituted 63.4% of the non-diabetic participants.

Discussion

In this study, the prevalence of non-diabetic PN was 21.5%, compared to 38.1% in the participants who suffered from diabetes. This finding is consistent with a study in the U.S., where the prevalence of DPN was higher than non-diabetic PN [10]. A greater proportion of the participants did not suffer from CVD (93.2%), while only a small proportion had a history of CVD (6.8%). Most of the participants (59.1%) earned a monthly income of TT\$ 2470-9800 (USD 364 -1,445), while a lesser proportion (40.9%) earned monthly income of over TT\$ 9800 (over USD 1,445). Furthermore, 94% of the participants were non-smokers, while only 6% smoked (OR, 1.13, $p > .05$, 95% CI: 0.27 – 4.80). Although there was an increased odds of developing non-diabetic PN from smoking, this association was not significant in this study, probably because most of the participants in this study were non-smokers.

The majority of the participants consumed alcohol (51.9%), while a lesser proportion had no history of alcohol consumption (48.1%). Majority of the participants in this study were females (63.4%), while males constituted a lesser proportion (36.6%). For the variable age, 51.1% of the participants were between 50-79 years, 45.9% of the participants constituted the age range 18-49 years, while 3% of the participants were aged 80 years and over. The majority of the participants in this study were Blacks (49.8%), East Indians (24.7%), and Others (25.5%).

CVD and participants’ age were significantly associated with the development of non-diabetic PN in the multivariate logistic regression analysis, while controlling for the other variables. There are no previous studies conducted in Trinidad and Tobago and the Caribbean to compare this finding with. However, DPN, a complication of diabetes is more prevalent in the CVD group [3]. This makes the finding of the association between CVD and non-diabetic PN in this study a novel one. The mechanism of the association between CVD and non-diabetic PN in this study is unclear, since important confounders of this association (smoking and alcohol consumption) were adjusted for in this study. The significant association between age and non-diabetic PN is consistent with findings in other parts of the world, where advancing age was associated with the development of non-diabetic PN [16]. A possible explanation for this could be that many disease processes occur probably because of the accumulation of a wide variety of cellular and molecular damage over time. The lack of an association between non-diabetic PN and income in this study was unexpected, considering that low income has been linked to poor health outcomes [14]. In this study, there was no association between smoking and alcohol consumption and the development of non-diabetic PN. This finding

was quite unexpected, since smoking and alcohol consumption have been associated with the development of non-diabetic PN in previous studies [6]. Because the society in Trinidad and Tobago is multiethnic, we examined the association between non-diabetic PN and the major ethnic groups. However, we found no association between non-diabetic PN and ethnicity in this study.

Limitations

The diagnosis of non-diabetic PN was self-reported in this study. Recall bias on the part of the participants could have limited this process. Although a simple description of non-diabetic PN, including the signs and symptoms, was clearly attached to the questionnaire, participants with low literacy level might have encountered challenges in accurately interpreting the description. This situation could have affected the prevalence of PN (both diabetic and non-diabetic) estimated in this study.

Implications

This study has implications for the discipline of public health and healthcare. In this study, the prevalence of PN among participants who did not suffer from diabetes was 21.5%, which is quite high. The findings from this study have implications for the management of patients suffering from CVD, but who do not suffer from diabetes. PN is insidious in onset and can be difficult to diagnose in the early stages. Patients with CVD who do not suffer from diabetes should be aggressively screened for PN. If PN is suspected or diagnosed among these patients, they should be properly managed for their PN, as PN is associated with significant mortality and morbidity. Timely and aggressive management of these patients can improve their health outcomes.

Recommendations for Further Research

In this study, there was a significant association between the development of CVD and non-diabetic PN. Future research on this topic should be conducted by employing larger studies to characterize and better understand the mechanisms or pathogenesis behind this association.

Conclusions

The prevalence of non-diabetic PN among participants from this study was 21.5%. This prevalence is quite high and should serve as a reminder for healthcare professionals to aggressively screen and manage people who do not suffer from diabetes, but who present with early signs and symptoms of PN, in order to improve their health outcomes. Furthermore, there was a significant association between CVD and non-diabetic PN. Patients with CVD who do not suffer from diabetes should be aggressively screened for PN. If PN is suspected or diagnosed among these patients, they should be properly managed for their PN, as PN is associated with significant mortality and morbidity.

Conflict of Interest: None.

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