Original Article

The changeable dynamics between glycaemic control and neuropathy risk across the lifespan of Saudi diabetic patients; A survey in diabetes healthcare facility

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Abstract

Background and Aims: Peripheral neuropathy is a common diabetic complication. It is linked to poor glycaemic control and longer duration of diabetes. We explored the association between HbA1c and neuropathy risk considering the duration of diabetes in a sample of Saudi diabetic patients. **Method:** We conducted a monofilament test on 343 diabetic patients referred to our specialist diabetology centre in Saudi Arabia. We utilized a multiple generalized logistic regression model with a binary outcome related to neuropathy complications. **Results:** We found that over four out of every five patients have peripheral neuropathy. The interaction between HbA1c and duration was significant (estimate = −0.02802, $P = 0.00534$), a positive association between neuropathy and both HbA1c (increased risk by 46.2%, $P = 0.03222$) and DM duration (increased risk by 19.6%, $P = 0.04497$). **Conclusions:** The shorter the duration of diabetes, the more positive the relationship between HbA1c and peripheral neuropathy. In patients living for over 40 years with diabetes, HbA1c was higher among those who did not have peripheral neuropathy. It could be argued that this is an artefact of survival as poorer glycaemic control will likely result in higher mortality in earlier years of the diabetes career.

Keywords: Diabetes, glycaemic control, monofilament test, peripheral neuropathy, Taif, Saudi Arabia

Introduction

Peripheral neuropathy is one of the most common complications of both type 1 and type 2 diabetes. According to WHO, Saudi Arabia occupies the second rank in diabetes in the Middle East and seventh worldwide.[1] Peripheral neuropathy is the most frequent neurological disorder that a diabetic patient presents to their treating clinicians.[2] Prevalence estimates revolve around one in every five diabetic subjects, although variations occur due to heterogeneous settings and sampling techniques.[3] Population-based studies estimated that 22% of diabetic patients would have moderate-to-severe peripheral neuropathy at any point in time,[4] and 50% would develop the condition over time.[5] Primary care physicians are the first line in the assessment and management of diabetes complications, including neuropathy.

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Patients living with diabetes develop a long-term relationship with their family physician. Therefore, understanding how complications develop throughout the duration of diabetes is central to the efficiency and effectiveness of care provided by general practitioners. This study aims to estimate the point prevalence of neuropathy among high-risk diabetic patients presenting at the diabetic and endocrine specialist centre in Prince Mansour Hospital and evaluate its associated factors.

Method

This study was a cross-sectional questionnaire-based descriptive survey of a random sample of type 2 diabetic patients who attended specialist diabetes and endocrine centre in Prince Mansour Military Hospital between January and May 2020 in Taif, Saudi Arabia. All patients over 20 and under 85 were included. A standard questionnaire included various socio-demographic and clinical factors and data pertaining to different podiatric parameters related to neuropathy that help ascertain the severity of neuropathy if present.

Data were analysed using the R-Statistical Software version 3.4.1. The adjusted effect of categorical variables on the outcome variable was determined using multiple generalized linear logistic regression modelling.

Results

The total number of participants included in the study was (n = 343) patients with diabetes. There were (n = 92, 26.8%) males and (n = 251, 73.2%) females. The mean age for the participating patients was 59.6 years (Standard Deviation (SD) = 10.4 years). As detected by the monofilament test, the prevalence of neuropathy was (n = 291) 84.8% diabetic patients.

Dyslipidaemia was associated with a higher risk for neuropathy by 98.4% (estimate = 0.6853, $P = 0.04614$). Additionally, lesser neuropathy risk was associated with cardiovascular disease by 62.1% (estimate = −0.9705, $P = 0.03516$), and retinopathy by 60.9% (estimate = −0.9401, $P = 0.00782$).

Interaction existed between the duration of diabetes and HbA1c levels in terms of their effect on peripheral neuropathy, as detailed in Table 1 and Figure 1. Clearly, in patients with a short duration of diabetes, a high HbA1c was associated with an increased probability of neuropathy. When interaction term is included, a positive association between neuropathy and both HbA1c (increased risk by 46.2%, estimate = 0.3798, $P = 0.03222$) and DM duration (increased risk by 19.6%, estimate = 0.1792, $P = 0.04497$) was noted.

Discussion

We found that over four out of every five patients have neuropathy complications. This is worrying as peripheral neuropathy can lead to an array of serious diabetic complications.[6] Our results far exceed the recent 30.1% neuropathy figure among primary care diabetic patients obtained by Sendi *et al.*[7] Our study was conducted among a high-risk group of attendees at the specialist diabetic centre.

Table 1: Logistic regression results for interaction between HbA1c and diabetes duration on risk of peripheral neuropathy

	Estimate	SE	*Z*	*P*
HbA1c level	0.37980	0.17734	2.142	0.03222*
DM duration	0.17920	0.08938	2.005	0.04497*
HbA1c-DM duration interaction	−0.02802	0.01006	−2.786	0.00534**

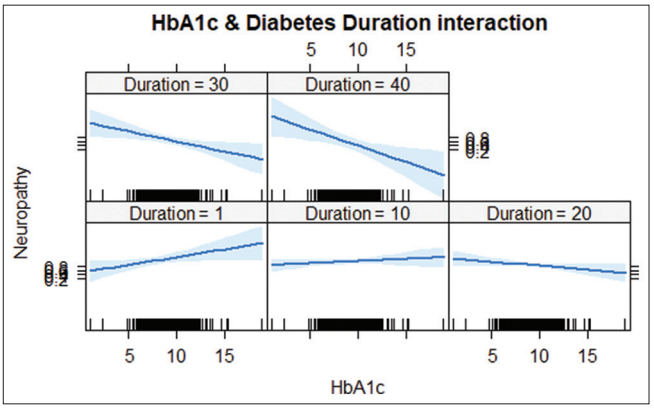

Figure 1: Interaction between HbA1c and duration of DM with respect to the effect on peripheral neuropathy

Literature from Saudi Arabia indicates an established link of diabetic peripheral neuropathy with the severity and duration of poor diabetic control.[8] In our investigation, we found that dyslipidaemia doubled the risk for neuropathy. Evidence packs a positive association between lipid profile and diabetic neuropathy.[9]

The link between dyslipidaemia and neuropathy extends even to non-diabetic subjects.[10] This confirms a direct nerve-damaging effect for high levels lipoproteins and lipids in the blood. The exact underlying bio-molecular mechanisms for how such damage is triggered, maintained, and progressed remain unclear. Recent directions of inquiry point towards the involvement of disordered mitochondrial functioning are caused by elevated levels of fatty acids.[11] The proposed mitochondrial impairments are induced depolarization, dysfunctional bioenergetics, and inefficient axonal transport.[11]

We uncovered a positive association between neuropathy and both HbA1c and DM duration. It is widely accepted that hyperglycaemia worsens sensorimotor nerve dysfunction.[12]

One further unexpected finding in our current survey is the association between cardiovascular disease and reduced risk of neuropathy. Diabetes is notorious for masking the symptomatology of cardiovascular disorders.[13] Over half of diabetic patients are estimated to have a silent cardiovascular disorder that can only be picked up during routine screening,[14]

with grave implications in denial and/or delay of necessary treatment to such severe life-threatening illnesses.[15] Clearly, in Saudi Arabia, the relationship between diabetes and cardiovascular disease was quite close, and the burden of cardiovascular morbidity was estimated to be 'exponential' in diabetic patients.[16] One of the most recently proposed molecular mechanisms involved in orchestrating vascular and neurological complications in diabetes is a calcium channel called 'transient receptor potential vanilloid 4'.[17]

The strengths of our study include a large sample size, data from attendees of a specialist diabetes centre, and a substantial response rate. However, several limitations must be acknowledged; the cross-sectional observational design would not allow for generalizability of findings. Our sample is a high-risk tertiary centre group and will over-represent diabetic complications. Moreover, the reliance on self-reported cardiovascular and ophthalmologic symptoms may have distorted the findings of the risk factor.

Future research is to adopt a longitudinal design to examine the survival of diabetic patients and its relationship to clinical factors. Molecular mechanisms can be elucidated by laboratory-based research that can be developed and nurtured in our centre at Taif.

Recommendations

1. Poor glycaemic control, poor lipid profile, and longer duration for diabetes remain the main factors affecting neurological complications of diabetes in Saudi Arabia and should be addressed by clinicians as early as patients present at healthcare facilities.
2. Research on diabetes complications in Saudi Araba should focus on the demographic and clinical factors affecting mortality and survival from diabetes.

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Conflicts of interest

There are no conflicts of interest.

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