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Foot complications in Type 2 diabetes: an Australian population-based study

R. J. Tapp, J. E. Shaw, M. P. de Courten, D. W. Dunstan, T. A. Welborn* and P. Z. Zimmet on behalf of the AusDiab Study Group

International Diabetes Institute, Melbourne, Australia
*Department of Medicine, University of Western Australia, Perth Australia

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Abstract

Aims To determine the prevalence and risk factors for neuropathy and peripheral vascular disease (PVD) in the Australian diabetic population and identify those at high risk of foot ulceration.

Methods The Australian Diabetes Obesity and Lifestyle study included 11 247 adults aged ≥ 25 years in 42 randomly selected areas of Australia. Neuropathy and PVD were assessed in participants identified as having diabetes (based on self report and oral glucose tolerance test), impaired fasting glucose, impaired glucose tolerance and in a random sample with normal glucose tolerance (total $n = 2436$).

Results The prevalence of peripheral neuropathy was 13.1% in those with known diabetes (KDM) and 7.1% in those with newly diagnosed (NDM). The prevalence of PVD was 13.9% in KDM and 6.9% in NDM. Of those with diabetes, 19.6% were at risk of foot ulceration. Independent risk factors for peripheral neuropathy were diabetes duration (odds ratio (95% CI) 1.73 (1.33–2.28) per 10 years), height (1.42 (1.08–1.88) per 10 cm), age (2.57 (1.94–3.40) per 10 years) and uric acid (1.59 (1.21–2.09) per 0.1 mmol/l). Risk factors for PVD were diabetes duration (1.64 (1.25–2.16) per 10 years), age (2.45 (1.86–3.22) per 10 years), smoking (2.07 (1.00–4.28)), uric acid (1.03 (1.00–1.06) per 0.1 mmol/l) and urinary albumin/creatinine ratio (1.11 (1.01–1.21) per 1 mg/mmol).

Conclusions The prevalence of neuropathy and PVD was lower in this population than has been reported in other populations. This may reflect differences in sampling methods between community and hospital-based populations. Nevertheless, a substantial proportion of the diabetic population had risk factors for foot ulceration.

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Keywords diabetic foot complications, epidemiology, neuropathy, peripheral vascular disease

The AusDiab Steering Committee consists of: Dr B. Atkins, Dr S. Bennett, Dr S. Chadban, Professor S. Colagiuri, Dr M. de Courten, Dr M. D'Embden, Dr D. Dunstan, Professor T. Dwyer, Dr D. Jolley, Dr P. Magnus, Professor J. Mathews, Dr D. McCarty, Professor K. O'Dea, Dr P. Phillips, Dr P. Popplewell, Mr I. Kemp, Professor H. Taylor, Professor T. Welborn and Professor P. Zimmet.

Correspondence to: Ms Robyn Tapp, The International Diabetes Institute, 250 Kooyong Road, Caulfield, 3162, Vic, Australia. E-mail: rtapp@idi.org.au

Abbreviations ABPI, ankle brachial pressure index; BMI, body mass index; ECQ, Edinburgh claudication questionnaire; HbA_{1c}, glycated haemoglobin; HDL, high-density lipoprotein; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; KDM, known diabetes mellitus; LDL, low-density lipoprotein; NDM, newly diagnosed diabetes mellitus; NDS, neuropathy disability score; NGT, normal glucose tolerance; NSS, neuropathy symptom score; OGTT, oral glucose tolerance test; PPT, pressure perception test; PVD, peripheral vascular disease; SD, standard deviation; WHO, World Health Organization

Introduction

Peripheral neuropathy and peripheral vascular disease (PVD) are common long-term complications of diabetes, and although a proportion of people with peripheral neuropathy and PVD have severe and debilitating pain, many are asymptomatic [1]. However, despite the lack of symptoms, people with neuropathy and PVD are at high risk of foot ulceration, infection and amputation [2–4]. Diabetic neuropathy and PVD are the main causes of non-traumatic lower limb amputation [5–7].

Only a limited number of population-based studies of diabetic neuropathy and foot complications have been conducted, and of these, very few have involved people with both previously and newly diagnosed diabetes [8,9]. Testing methods for neuropathy have varied from simple assessment of pin-prick perception through to assessment using several different scales [10,11]. However, in 1988 the San Antonio conference released a consensus statement on the diagnosis of diabetic neuropathy [12]. It recommended using at least one measure from each of the following categories: clinical symptoms, clinical signs, neurophysiology, quantitative sensory testing and autonomic function tests. In epidemiological research this has been difficult to implement, and a variety of definitions of neuropathy have been adopted.

The variation in definition has contributed to differences in the prevalence reported, further influenced by the majority of studies using hospital-based populations. Hospital-based clinic populations differ according to referral patterns and tend to over-represent the more severe disease states. Nevertheless, there have been some consistent findings that suggest the prevalence of neuropathy in a hospital-based clinic setting is approximately 30% [13,14], while in population-based studies, which include screening with the oral glucose tolerance test (OGTT), it is nearer to 10% (known and newly diagnosed diabetes combined) [8,9]. The prevalence of PVD has also been quite variable, depending upon the definition adopted, age, location and sex of participants [15].

Within Australia, no national study of diabetic foot complications has previously been undertaken. In the first national population-based diabetes survey of Australia in 1999–2000 (the Australian Diabetes Obesity and Lifestyle study (AusDiab)), diabetes was found in 7.4% of adults aged ≥ 25 years [16]. This study measured neuropathy, PVD and history of foot ulceration with the aim of determining the prevalence and risk factors in the Australian population and to identify those at high risk of foot ulceration.

Patients and methods

Sample selection

The population, methods and response rates of the AusDiab study are found in detail elsewhere [17]. In brief, the AusDiab study was a cross-sectional, population-based survey of 11 247 adults aged ≥ 25 years residing in randomly selected urban and rural areas of Australia. A stratified cluster sampling method was used, involving seven strata (six states and Northern Territory), and clusters were based on census collector districts. The sample size was selected based on estimates to identify a national diabetes prevalence of 7% (an estimate based on the results of previous surveys and the expectation that the diabetes rate had increased over time). Of those who completed a household interview 55.3% attended the biomedical examination. Diabetes classification was based on a 75-g OGTT, using the 1999 WHO diabetes classification [18]. Diabetes was diagnosed on the basis of fasting plasma glucose of ≥ 7.0 mmol/l or 2-h plasma glucose of ≥ 11.1 mmol/l or on current treatment with insulin or oral hypoglycaemic medication. Impaired glucose tolerance (IGT) was defined on the basis of fasting plasma glucose of < 7.0 mmol/l and 2-h plasma glucose of ≥ 7.8 and < 11.1 mmol/l and impaired fasting glucose (IFG) on the basis of fasting plasma glucose of ≥ 6.1 and < 7.0 mmol/l and 2-h plasma glucose of < 7.8 mmol/l. Those with self-reported diabetes and either on current treatment (insulin or oral hypoglycaemic medication) or with diabetic glucose values were categorized as having known diabetes (KDM). Participants diagnosed with diabetes through the AusDiab study were categorized as newly diagnosed (NDM). Type 1 diabetes required insulin treatment to have been started within 2 years of diagnosis (if diabetes onset was at age 40 or later, current body mass index (BMI) had to be < 27 kg/m^2). All other cases were classified as Type 2. Participants from the AusDiab study identified as having diabetes, IGT, IFG, and a random sample of participants with normal glucose tolerance (NGT), were eligible to attend the complications study. Participants with NGT were selected using a systematic random sample selecting every nth person. The nth person was dependent upon the number of people expected on the day of testing, in order to obtain a sample size of 10 per day. Of 2773 participants invited to the complications component, 2476 attended (overall response rate

89%; 91% in those with diabetes and 88% in those without diabetes) and data were available on 2468 participants. There were 430 people with KDM, 423 with NDM, 1151 with IGT or IFG and 464 with NGT. Thirty-two out of 430 of those with KDM had Type 1 diabetes and were excluded from this analysis. Overall there were no significant differences in sex or mean age between those who attended and did not attend the study. Among those with diabetes (known and newly diagnosed), 52% of attendees were male and 65% of the non-attendees were male ($P = 0.018$), but there was no significant difference in mean age between those who attended and did not attend the study.

Measures

Four scales were used to classify neuropathy. The modified neuropathy symptom score (NSS), modified neuropathy disability score (NDS), pressure perception test (PPT) and postural blood pressure drop. The NSS included questions about burning, numbness, tingling, aching, and cramp-like pain or discomfort in legs or feet [13]. The NDS examined ankle reflexes, vibration perception on the great toe, pin-prick perception (using standard neurotips) on the dorsal surface of the great toe and temperature perception on the dorsal surface of the metatarsal heads [13]. Pressure perception was assessed using a 10-g monofilament. Three sites were tested on the plantar surface of each foot—the great toe, 1st and 5th metatarsal heads [19]. If the monofilament was not felt, the test was repeated twice, and a score of sensate was only recorded if both retests were correct. Areas of callus were avoided. All sensory testing was demonstrated on the forearm, and eyes were closed throughout. Lying blood pressure was measured on the right arm with a standard sphygmomanometer after the participant had rested in a supine position for 10 min. The arm was measured to ensure the correct sized cuff was used. Blood pressure was measured again after standing for 60 s. Blood pressure was assessed with the first and fifth Korotkoff sounds to the nearest 2 mmHg [20]. Hypertension was defined as present if the systolic blood pressure was ≥ 140 mmHg, the diastolic blood pressure ≥ 90 mmHg or the participant reported current treatment for hypertension. Neuropathy was defined as present if two or more of the four scales were abnormal, NSS > 4, NDS > 5, PPT < 6 (each site scored as 1 if normal and 0 if abnormal), fall in systolic blood pressure of ≥ 20 mmHg. These cut-offs were determined from previously published data [13,19,20]. Population-based age and sex-specific normal ranges were also calculated for each of the four neuropathy scales.

The ankle brachial pressure index (ABPI) and the Edinburgh Claudication questionnaire (ECQ) were used to classify PVD [21,22]. PVD was defined as asymptomatic if the ECQ requirements for claudication were not met [22]. The ABPI was defined as ankle pressure/arm pressure (normal ≥ 0.9) and measured on the right side using a standard sphygmomanometer and a Doppler probe (model D900; Huntleigh Diagnostics, Cardiff, UK) after resting for 5 min. The systolic pressure was measured at the brachial artery and then at the posterior tibial or dorsal pedis artery of the foot (two recordings were taken at each site and the average of the two readings was used in the analyses). The ECQ and history of foot ulceration were determined through an interviewer-administered questionnaire. Foot risk was defined by the presence of any one of neuropathy, decreased pressure perception, ABPI < 0.9 or history of foot ulceration.

Other measures

Height and weight were measured in light clothing without shoes. BMI was calculated as weight (kg)/height (m^2). Information on alcohol consumption, smoking, medication and history of diabetes was obtained by interview. Plasma glucose was measured by the glucose oxidase method using the Olympus AU600 analyser. Serum total cholesterol, HDL-cholesterol, triglycerides and uric acid were determined by enzymatic methods (Olympus AU600 analyser). Urinary albumin and creatinine were also determined by enzymatic methods (Olympus AU600 analyser). C-peptide was measured by radioimmunoassay (Linco, St Charles, MO, USA). HbA_{1c} was measured in whole blood using boronate affinity high-performance liquid chromatography (BioRad Variant Haemoglobin Testing System). The normal range for HbA_{1c} is 4.2–6.3%.

The study was approved by the ethics committee of the International Diabetes Institute. Informed consent for the study was obtained from all participants.

Statistical analysis

Data analysis was performed with STATA version 7.0 for Windows (STATA Inc., 2001; TX, USA). Descriptive information for each of the variables was derived and distribution assessed. Triglyceride values were log transformed (to correct for skewness) and are presented as geometric mean ×/÷ antilogged SD. In order to determine normal ranges for each of the four neuropathy scales, the data from 1122 non-diabetic participants were combined (after excluding those with a high alcohol intake). The upper limit of normal for each of three age groups (25–39, 40–59, 60+ years) was then calculated separately for males and females as the 95th percentile of the age- and gender-specific distribution. Univariate associations with neuropathy and PVD were assessed using independent sample *t*-tests for continuous variables (Mann–Whitney test was used for HbA_{1c}, urinary albumin/creatinine ratio and diabetes duration as the data were skewed; those with newly diagnosed diabetes were given a diabetes duration of 0 years) and χ^2 for categorical variables. Variables with $P \leq 0.25$ from the univariate analysis and established risk factors were selected for entry into logistic regression models using a backwards method.

Results

The prevalence of neuropathy and PVD by diabetes status is shown in Table 1. The prevalence of neuropathy in people with diabetes (KDM and NDM combined) was 10.0% and increased with diabetes duration (< 5 years 7.9%; 5–9 years 14.7%; 10–19 years 13.3%; and ≥ 20 years 28.1%). The prevalence of neuropathy using the population-defined age and sex-specific normal ranges was 4.9% in those with diabetes (7.0% in those with KDM and 2.8% in those with NDM; Table 1) and the prevalence increased with duration of diabetes (< 5 years 3.3%; 5–9 years 7.4%; 10–19 years 8.4%; and

Table 1 Prevalence of neuropathy and peripheral vascular disease (PVD) by glucose tolerance status

		Neuropathy		PVD		
	n	Standard definition	Defined from derived age- and sex-specific normal ranges	ABPI < 0.9	Positive claudication history	ABPI < 0.9 or positive claudication history
NGT	464	2.8 (1.5–4.7)	1.3 (0.5–2.8)	1.9 (0.9–3.6)	1.9 (0.9–3.6)	3.2 (1.8–5.3)
IFG	142	5.6 (2.5–10.8)	0.7 (0.02–3.9)	2.8 (0.7–7.1)	3.5 (1.2–8.0)	5.6 (2.5–10.8)
IGT	1009	5.7 (4.4–7.4)	1.9 (1.1–2.9)	3.2 (2.2–4.4)	4.3 (3.1–5.7)	6.3 (4.8–7.9)
NDM	423	7.1 (4.8–10.0)	2.8 (1.5–4.9)	4.3 (2.5–6.7)	3.6 (2.0–5.8)	6.9 (4.7–9.7)
KDM	398	13.1 (9.9–16.8)	7.0 (4.7–10.0)	8.6 (6.0–11.8)	7.6 (5.2–10.6)	13.9 (10.6–17.7)

Data are numbers or percentages (95% confidence intervals).
NGT, Normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NDM, newly diagnosed diabetes; KDM, known diabetes; ABPI, ankle brachial pressure index.

Table 2 Risk of peripheral vascular disease by glucose tolerance status

	Model 1		Model 2		Model 3	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
NGT	1.00		1.00		1.00	
IFG	1.82 (0.76–4.40)	0.182	1.74 (0.71–4.27)	0.224	1.68 (0.68–4.16)	0.259
IGT	1.88 (1.06–3.35)	0.032	1.37 (0.76–2.46)	0.300	1.37 (0.75–2.49)	0.304
NDM	2.04 (1.07–3.89)	0.031	1.29 (0.67–2.50)	0.449	1.18 (0.60–2.35)	0.628
KDM	4.79 (2.66–8.63)	< 0.001	2.92 (1.59–5.34)	0.001	2.55 (1.36–4.79)	0.004

NGT, Normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NDM, newly diagnosed diabetes; KDM, known diabetes.
Model 1 unadjusted; model 2 adjusted for age and sex; model 3 adjusted for age, sex, cholesterol, triglycerides, body mass index, smoking and systolic blood pressure.

≥ 20 years 18.8%). The prevalence of PVD (ABPI < 0.9 or claudication present) in people with diabetes (known and newly diagnosed) was 10.3% and also increased with diabetes duration (< 5 years 7.5%; 5–9 years 15.8%; 10–19 years 16.9%; and ≥ 20 years 31.3%). Among those with diabetes (KDM and NDM), PVD (defined by ABPI < 0.9) was asymptomatic in 74% (81.1% of those with ABPI 0.70–0.89 and 53.8% of those with ABPI < 0.7) and was asymptomatic in 63.6% of those without diabetes (IGT, IFG and NGT). However, the difference was not significant ($P = 0.278$). For those with previously diagnosed diabetes, the excess risk of having PVD was only partially attenuated by adjustment for other cardiovascular risk factors (Table 2). For those with newly diagnosed diabetes as well as for lesser degrees of glucose intolerance, the increased risk of PVD was removed once age and sex were adjusted for. Of those with diabetes and peripheral neuropathy, 23.2% also had PVD. There were several participants with an ankle pressure ≥ 300 mmHg due to incompressibility of the arteries [23] (KDM = 9, NDM = 3, IGT = 3, IFG = 1 and NGT = 2), and of these participants three were classified with PVD using the ECQ.

Previous foot ulceration was reported by 2.1% of people with diabetes (3.0% KDM and 1.2% NDM; $P = 0.108$). Risk factors for foot ulceration were more common amongst those with KDM than those with NDM (24.1% vs. 15.3%; $P = 0.002$). Of people with diabetes (known and newly diagnosed), 19.6% were at risk of foot ulceration, with the greatest risk evident in those with a diabetes duration ≥ 20 years (< 5 years 16.6%; 5–9 years 22.1%; 10–19 years 26.5%; and ≥ 20 years 53.1%).

Table 3 shows the univariate associations of possible risk factors with neuropathy. Participants with neuropathy were significantly older, had a longer duration of diabetes, higher systolic blood pressure and uric acid levels compared with participants without neuropathy. Height, age, systolic BP, duration of diabetes, HbA_{1c}, sex, BMI, cholesterol, urinary albumin/creatinine ratio, smoking and uric acid were entered into a logistic regression model. From the model, diabetes duration, age, height and uric acid were identified as independent risk factors for neuropathy (Table 4). When population-defined normal ranges were used to classify neuropathy, duration of diabetes, uric acid and height were identified as independent risk factors for neuropathy.

Table 5 shows the univariate associations of risk factors with PVD. Univariate risk factors for PVD included age, duration of diabetes, urinary albumin/creatinine ratio, hypertension,

Table 3 Univariate associations with neuropathy (in those with new and previously diagnosed diabetes)

	Neuropathy	No neuropathy	*P*-value
n	82	739	
Age (years)	73 ± 10	62 ± 12	< 0.001
Male (%)	55	51	0.463
Height (cm)	167 ± 10	166 ± 9	0.141
Body mass index (kg/m^2)	29.3 ± 6.5	30.2 ± 6.0	0.241
Waist circumference (cm)	103 ± 17	101 ± 14	0.332
Duration of diabetes (years)*	2.5 (0–9.5)	0 (0–4)	< 0.001
Current smoker (%)	8	12	0.207
HbA_{1c} (%)	6.3 (5.7–7.4)	6.1 (5.6–7.1)	0.197
C-peptide (ng/ml)	3.8 ± 1.7	3.8 ± 1.7	0.955
Uric acid (mmol/l)	0.36 ± 0.1	0.33 ± 0.1	0.001
Current alcohol drinker (%)	66	72	0.320
Urinary albumin/creatinine ratio (mg/mmol)	1.7 (0.9–14.5)	1.0 (0.6–2.5)	< 0.001
Hypertension (%)	82	67	0.005
Systolic BP (mmHg)	149 ± 20	141 ± 20	0.001
Diastolic BP (mmHg)	77 ± 11	78 ± 9	0.150
Lipid treatment (%)	28	26	0.909
Cholesterol (mmol/l)	5.5 ± 1	5.7 ± 1	0.168
Triglycerides (mmol/l)	1.9 ×/÷1.8	1.9 ×/÷1.7	0.954

Data given as mean ± SD, geometric mean ×/÷ SD, median (interquartile range).
*Newly diagnosed participants given duration of zero.

Table 4 Final logistic regression models for peripheral neuropathy

	KDM and NDM		KDM only	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Diabetes duration (per 10 years)	1.73 (1.33–2.28)	< 0.001	1.68 (1.19–2.35)	0.003
Height (per 10 cm)	1.42 (1.08–1.88)	0.012	1.93 (1.34–2.80)	< 0.001
Age (per 10 year)	2.57 (1.94–3.40)	< 0.001	2.60 (1.77–3.81)	< 0.001
Uric acid (per 0.1 mmol/l)	1.59 (1.21–2.09)	0.001	2.10 (1.45–3.05)	< 0.001

KDM, Known diabetes mellitus; NDM, newly diagnosed diabetes mellitus.

Table 5 Univariate associations with peripheral vascular disease (PVD) (in those with new and previously diagnosed diabetes)

	PVD	No PVD	*P*-value
*n**	84	733	
Age (years)	72 ± 11	62 ± 12	< 0.001
Male (%)	54	51	0.624
BMI (kg/m^2)	28.4 ± 5.5	30.3 ± 6.1	0.006
Waist circumference (cm)	100 ± 14	101 ± 15	0.221
Duration of diabetes (years)†	4 (0–10)	0 (0–4)	< 0.001
Current smoker (%)	15	12	0.444
HbA_{1c} (%)	6.1 (5.7–7.8)	6.1 (5.6–7.1)	0.131
C-peptide (ng/ml)	3.6 ± 1.8	3.8 ± 1.7	0.425
Uric acid (mmol/l)	0.34 ± 0.10	0.33 ± 0.1	0.123
Current alcohol drinker (%)	69	71	0.619
Urinary albumin/creatinine ratio (mg/mmol)	1.9 (0.9–14.5)	1.0 (0.6–2.5)	< 0.001
Hypertension (%)	81	66	0.007
Systolic BP (mmHg)	150 ± 20	141 ± 20	< 0.001
Diastolic BP (mmHg)	76 ± 9	78 ± 10	0.026
Lipid treatment (%)	46	24	< 0.001
Cholesterol (mmol/l)	5.4 ± 1.0	5.7 ± 1.0	0.034
Triglycerides (mmol/l)	1.9 ×/÷ 1.7	1.9 ×/÷ 1.7	0.944

Data given as mean ± SD, geometric mean ×/÷ SD, median (interquartile range).
*The total *n* differs from that given in Patients and Methods, as four people had incomplete PVD data.
†Newly diagnosed participants given duration of zero.

Table 6 Final logistic regression models for peripheral vascular disease

	KDM and NDM		KDM only	
	Odds ratio (95% CI)	*P*-value	Odd ratio (95% CI)	*P*-value
Diabetes duration (per 10 years)	1.64 (1.25–2.16)	< 0.001	1.45 (1.05–2.00)	0.024
Urinary albumin/creatinine ratio (per 1 mg/mmol)	1.11 (1.01–1.21)	0.030	1.10 (1.01–1.21)	0.036
Age (per 10 years)	2.45 (1.86–3.22)	< 0.001	2.38 (1.67–3.39)	< 0.001
Uric acid (per 0.1 mmol/l)	1.03 (1.00–1.06)	0.048	1.04 (1.00–1.08)	0.041
Current smoker	2.07 (1.00–4.28)	0.049		

lower BMI, and cholesterol. Age, duration of diabetes, urinary albumin/creatinine ratio, systolic BP, BMI, cholesterol, sex, HbA_{1c}, uric acid and smoking were entered into a logistic regression model. From the logistic regression model, diabetes duration, age, smoking, uric acid and urinary albumin/creatinine ratio were identified as independent risk factors for peripheral vascular disease (Table 6).

Discussion

This was one of the first population-based studies of diabetic foot complications and one of very few in which the diabetic population was defined by an OGTT. This is important, because the prevalence of complications depends largely upon how a population has been defined. By using the OGTT the population is less biased toward those with severe disease, as those with both diagnosed and previously undiagnosed diabetes are included. Furthermore, this methodology enhances the ability to make comparisons with other similar studies. When studies are restricted to people with known diabetes, the calculated prevalence of any diabetic complication is partly dependent on the proportion of the total diabetic population that is diagnosed. However, when screening by OGTT is involved, the total diabetic population is defined, and this source of interstudy variability is removed.

The prevalences of peripheral neuropathy and PVD in this population were lower than have been reported in other populations. This may reflect differences in sampling methods between community and hospital-based populations, as well as methodological differences in testing. In the current study, neuropathy was found in 10.0% and PVD in 10.3% of those with diabetes. The low prevalence was not due to adopting newer diabetes diagnostic criteria [18], since the prevalences were also low in those with previously diagnosed diabetes. Furthermore, when using the 1985 WHO definition of diabetes [24] the prevalences of neuropathy and PVD rose to only 10.6% and 10.9%, respectively. In two similar studies (albeit in different ethnic groups) including known and newly diagnosed diabetes, the prevalence of neuropathy was shown to be 8.3% in Mauritius and 19.8% in Egypt [8,9]. Both of these studies limited the definition of neuropathy to vibration perception using a biothesiometer, and the latter defined neuropathy using a reference range derived from non-diabetic young adults, which may have led to an overestimate of the prevalence. A population-based study of PVD in India showed a prevalence of 6.3% among those with known and newly diagnosed diabetes [25] and a study from The Netherlands showed a prevalence of 17.3% (known and newly diagnosed diabetes, age limited to those 50–74 years) [26]. Most studies of PVD have limited testing to participants aged 45–75 years, used varying definitions of PVD and sampling techniques, making comparisons difficult [21,26].

The increased risk of cardiovascular disease (CVD) amongst those with diabetes is well established [27]. Although it has been generally accepted that those with diabetes have an increased risk of developing PVD, few population-based studies have focused on the prevalence of PVD by glucose tolerance [15,26,28]. While PVD is common in those with NGT [21], the present study suggests that those with KDM are at an increased risk of developing PVD, even after adjustment for traditional cardiovascular risk factors.

Evaluation of foot risk in the diabetic population is the main reason for assessing the prevalence of neuropathy and PVD. This study has shown that the 'at risk' foot became more common with increasing age and duration of diabetes. For those with a diabetes duration of ≥ 20 years, 53.1% had evidence of an 'at risk' foot.

Independent risk factors for neuropathy were height, uric acid, age and duration of diabetes. However, age was no longer an important factor when population-based normal ranges were used to define neuropathy. By defining age- and gender-specific normal ranges we controlled for the age-associated decline in neurological function, which occurs in both diabetic and healthy individuals. Apart from uric acid, these risk factors confirm the findings reported in other populations [9,11]. The association between uric acid and neuropathy has not been described previously. There is no obvious mechanism for this association, but hyperuricaemia has also been shown to be associated with early or increased progression to nephropathy [29] and is included as part of the metabolic syndrome [30]. Its association with neuropathy in the current study could be seen as lending support to the vascular hypothesis of diabetic neuropathy [31]. Many studies have shown height to be associated with neuropathy [32,33]. Height is associated with the length of axons and longer axons are more prone to metabolic disturbances [34,35]. In this study as with others,

gender was not shown to be an important factor for neuropathy, either as a risk factor or effect modifier [13].

Duration of diabetes is a well-established risk factor for neuropathy [9,36] and in this study remained important even after adjustment for age. HbA_{1c} was not a risk factor for neuropathy in this study when duration of diabetes was entered into the model. There have been conflicting results in other studies on the role of glycaemic control in the development of neuropathy [9,37–40]. The finding of the current study is consistent with the San Luis Valley Diabetes Study [40], which showed glycaemic control was related to peripheral neuropathy in multivariate modelling until duration of diabetes entered the model. Once duration of diabetes entered the model HbA_{1c} fell out. A population-based study from Mauritius showed no association between fasting plasma glucose and neuropathy in the cross-sectional analysis, but did show an association in the longitudinal analysis [9]. The UKPDS showed no consistent impact of glycaemic control on the development of neuropathy in Type 2 diabetes [38]. It may be that neuropathy is not as closely related to glycaemic control as are nephropathy and retinopathy. Alternatively, duration of diabetes may more closely represent total glycaemic exposure and, in modelling, the more precise measure would be included in the model, even though it may not be as closely associated with the outcome.

Independent risk factors for PVD in this study were duration of diabetes, age, smoking, uric acid and urinary albumin/creatinine ratio, confirming the findings reported in other populations [28,41,42]. Studies of CVD have frequently shown urinary albumin to be elevated in people with CVD [43,44]. However, the association between urinary albumin and PVD is not necessarily causal and may simply reflect common antecedents. It has been suggested that increased urinary albumin may be a marker for endothelial damage [45,46]. Endothelial function may therefore be the common cause of both microalbuminuria and PVD. Cholesterol showed no independent association with PVD even after those on lipid-lowering therapy were excluded (data not shown). This is consistent with some studies [26,47], although others have shown an association of lipids with PVD [1,42,48]. Smoking is a well-known risk factor for PVD [28]. The mechanism for this is not fully understood, though it is thought that smoking may promote LDL oxidation [49]. Duration of diabetes was a risk factor for PVD independent of age, which was also demonstrated to be an independent risk factor. HbA_{1c} was not found to be a risk factor for PVD. This has been shown previously [42,48]. The association of uric acid with PVD has not been shown previously, but an association has been shown in studies of CVD [50], and this may be related to its association with other components of the metabolic syndrome [30].

The ankle brachial pressure index and ECQ have been demonstrated to be reliable methods for detecting PVD [22]. However, the use of a Doppler probe in detecting PVD has limitations, since calcification of arteries occurs frequently in people with diabetes, leaving the arteries incompressible. This may have led to an underestimation of the prevalence of PVD in this population.

In conclusion, this cross-sectional, population-based study has shown diabetic neuropathy and PVD to be present in 10% and 10.3% of the diabetic population, respectively. Duration of diabetes was an important determining variable for both complications. In comparison with other published studies, the prevalence of peripheral neuropathy and PVD was quite low. This would appear to reflect differences in sampling methods between community and hospital-based populations as well as differences in testing methods. To our knowledge, this is the first population-based study to use a comprehensive definition of neuropathy. The most important reason for examining neuropathy and PVD is to assess risk of foot ulceration, and in this population a substantial proportion of the diabetic population had risk factors for foot ulceration. The costs of foot ulcers and amputations are extremely high [51,52], and given the rising prevalence of diabetes [53], the burden of foot complications is likely to remain high.

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