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Long-term complications in newly diagnosed Sri Lankan patients with type 2 diabetes mellitus

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Summary

We screened 597 newly-diagnosed diabetic patients (201 women) mean ± SD age 42.3 ± 6.2 years to determine the prevalence of diabetic complications; 22% presented because of symptoms of diabetes, 27% were diagnosed when hyperglycaemia was discovered at a health screening, and 36% were diagnosed while being treated for intercurrent illness. Neuropathy was present in 25.1%, nephropathy in 29%, retinopathy in 15%, coronary vascular disease in 21%, stroke in 5.6%, peripheral vascular disease in 4.8%, hypertension in 23%, obesity in 16%, central obesity in 21.3%, hypercholesterolaemia in 11%, hypertriglyceridaemia in 14%, and low high-density lipoprotein cholesterol in 12%. The prevalence of coronary vascular disease, hypertension, stroke, neuropathy and retinopathy at the time of diagnosis were higher in our patients than in Caucasian and Indo-Asian patients in the UK. Both a genetic predisposition to develop complications, and exposure to a longer duration of asymptomatic hyperglycaemia due to poor access to adequate health care, may contribute to the high frequency of complications at diagnosis. Since complications are already present at diagnosis, there is a case for implementing primary prevention programmes combined with screening for diabetes in high-risk groups.

Introduction

The WHO estimates that there are 40 million people with diabetes in developing countries, and that the number is expected to increase to 65 million by the year 2000.[1–5] The prevalence of diabetes in those aged 31–64 is 5.02%[6] for urban Sri Lanka and 2% in rural groups.[7]

Mortality and morbidity from macrovascular disease,[8] hyperlipidaemia,[9] and retinopathy[10] are high in Sri Lankan diabetic patients. This is especially so in the elderly.[11] Intervention in the form of integrated services provided by a diabetes health-care team in preventing complications is cost-effective in a Sri Lankan setting.[12–15] Prevention usually commences at diagnosis. However complications such as retinopathy and neuropathy have been found even at presentation.[10,16–18]

Apart from studies in immigrant populations,[19] no systematic studies are available regarding the prevalence of complications at diagnosis in Indo-Asian patients with type 2 diabetes. We conducted a study to determine the prevalence of diabetic complications in newly-diagnosed diabetic patients.

Methods

Primary-care (General) practitioners, in defined suburbs in the Greater Colombo area of Sri Jayawardenapura, Maharagama, Dehiwala Mount Lavinia, Ratmalana, Moratuwa, Nugegoda, Pannipitiya and Piliyandala were invited to participate in the study by referring all newly-diagnosed diabetic

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patients aged 25–65 years to a specialist diabetic clinic. The clinic was held on three days of the week. Patients were seen on the same day wherever possible, and all were seen within one week of referral.

Fasting plasma glucose was measured from a venous sample after an overnight fast from 2200 h. Blood glucose was assessed using the glucose oxidase method. If diabetes was confirmed, the patients were asked if they wished to participate in a study. Patients with ketonuria at presentation were excluded.

Participating patients were seen in clinics, held in the morning. A questionnaire was completed for each diabetic patient, on which name, age, sex, present age and date of diagnosis of diabetes were recorded. Smoking status was recorded as smoker, ex-smoker or non-smoker.

Macrovascular disease

A WHO questionnaire was used to assess the prevalence of macrovascular disease.[20] Blood pressure was measured recorded in the right arm supported on a table at heart level after 5 min rest. A mercury sphygmomanometer with a 23×14 cm cuff (bladder 23×13 cm) and a larger cuff for obese patients was used. The average of three readings was recorded as the blood pressure.[21] Hypertension was diagnosed according to WHO criteria. Those with systolic blood pressure >160 mmHg or diastolic blood pressure >95 mmHg, or who were taking antihypertensive medication were considered to have hypertension.

A 12-lead electrocardiogram was recorded in all patients. The results of ECG were grouped into three categories using a modified Minnesota code.[22] 'Coronary probable' included those with large Q or Qs waves and those with complete left branch bundle block (Minnesota codes 1-1, 1-2 and 7-1). 'Coronary possible' included those with small Q waves, ST-segment abnormalities and T-wave abnormalities. All other ECGs were regarded as normal. This ECG classification has been used in several studies.[23,24]

Stroke was diagnosed if patients had a history, residual neurological signs, hospital notes/discharge summaries or CT scans suggested a diagnosis of stroke.

Lipids

Venepuncture was performed after a 14-h fast in patients and controls. Serum was separated from blood samples within 2 h of collection. High-density lipoprotein (HDL) fraction was isolated for cholesterol analysis by the phosphotungstic acid and magnesium chloride method. Serum high-density lipoprotein (HDL) cholesterol and total cholesterol were estimated by the CHOD-PAP method and total triglycerides by the GPO-PAP method in an autoanalyzer (Cobas Mira) using commercially available test kits (Boerhinger Mannheim). Low-density lipoprotein (LDL) cholesterol was calculated in conventional units (mg/dL) using Freidwalds equation.[25] All lipid data were then converted to SI units. Dyslipidaemias were diagnosed using criteria recommended by the European Atherosclerosis Society.[26]

Anthropometry

Height without shoes was recorded in cm and weight without shoes was recorded in kg using a beam balance. Body mass index was calculated as BMI = weight in kg/height in metres^2 (kg/m^2). Obesity was defined as BMI >25 in women and >27 in men.[27] Waist and hip girths were measured with the subject standing, using a fibreglass tape with a spring balance attached to one end to hold the tape at a tension of 500 g. The waist was defined as the smallest girth between costal margin and illiac crests, and the hip as the circumference at the level of greater trochanters.[28] No data are available for central obesity in Sri Lanka, hence we used European values which defined central obesity (android fat distribution) as a

Table 1 Prevalence of complications

	Men	Women	Total
Number	396	201	597
Abnormal ECG (%)*	102 (25.7)	59 (29.3)	161 (26.9)
Hypertension (%)	97(24.4)	40 (19.9)	137 (23%)
Stroke (%)	20 (5)	11 (5.4)	31 (5.1)
Myocardial infarction (%)	31 (7.8)	13 (6.4)	44 (7.3)
Intermittent claudication (%)	21 (5.3)	7 (3.4)	28 (4.6)
Neuropathy (%)	107 (26.9)	44 (21.8)	151 (25.2)
Retinopathy (%)	54 (13.6)	37 (18.4)	91 (15.2)

* Coronary possible and probable.

waist:hip ratio above 1.0 in men and above 0.85 in women.[29,30]

Neuropathy

Patients were screened for neuropathy using established criteria.[31] All patients were questioned regarding symptoms of neuropathy using a neuropathy symptom score (NSS) using a previously-validated questionnaire.[32] Patients were asked if they experienced feelings of pins and needles, abnormal cold or warm sensations in their feet, sharp pain, aching pain, burning pain or irritation in feet or legs by bedclothes at night. Each symptom scored 1 point if present, and 2 if nocturnal exacerbation was present, giving a maximum of 10.

A modified neuropathy disability score (NDS) was used to diagnose and quantify the severity of diabetic neuropathy on clinical examination.[32] The ankle reflexes were scored as follows: 0, normal; 1, elicited with reinforcement; 2, absent. The sensations of pain, touch and vibration were tested in both feet. Each was scored as 0 for present and 1 for absent. The maximum score possible was 10. A NDS >6 was considered abnormal. Thus a patient with absent ankle reflexes alone would not be classified as neuropathy, but absent ankle reflexes with inability to feel at least one of the sensations tested would constitute neuropathy. Vibration perception threshold (VPT) was measured using a biothesiometer (Biomedical Instruments). Patients with abnormalities in NDS or NSS and VPT were considered to have neuropathy.

Retinopathy

Corrected visual acuity was recorded for each eye using a Snellens chart. Patients were requested to bring their spectacles for the eye test. Pinhole correction was used where spectacles were not brought. The definition of legal blindness was taken as visual acuity 6/60 or worse.

Fundus examination was performed after pupils were dilated to at least 3 mm. Optic fundi were examined by a consultant ophthalmologist, and graded according to criteria used for the WHO multinational study on diabetes.[33] In case of doubt, the ophthalmologist performed a fluorescein angiogram.

Nephropathy

Urine albumin, and creatinine were measured in a random urine sample. Urine albumin concentration was expressed relative to the mean urine creatinine concentration of 8 mmol/l in women and 11 mmol/l in men, to allow for urine dilution.

Results

We screened 597 patients (201 women) for complications at diagnosis. Mean $\pm$ SD age at presentation was 42.3 ± 6.2 years. Twenty-two percent of the patients presented because of symptoms of diabetes such as polyuria and loss of weight; 27% were diagnosed when hyperglycaemia was discovered at a health screening examination (pre-employment or in-service medical examinations for confirming employment or for insurance examinations); 36% were diagnosed while being treated for intercurrent illness such as angina, myocardial infarction hypertension, genital infections or cellulitis of the foot; 7% were diagnosed because of a complication such as blindness, end-stage renal disease, gangrene or neuropathic ulcer.

Ten per cent of males presented with balanitis and 2% of females with genital infections.

Symptomatic neuropathy was found in 9.8%; 2.6% presented with foot ulcers and 7.1% had signs of neuropathy (i.e. NDS >6). In all, 10% of patients had neuropathy on clinical criteria. All these patients had abnormal vibration perception on a biothesiometer; 15.1% had abnormal vibration perception without symptoms or signs.

The prevalence of abnormal ECG (coded 'coronary probable' and 'coronary possible') was 21%. Symptoms suggestive of a myocardial infarction were present in 7.4% of patients. Symptoms of angina were found in 11.2%. Stroke was present in 5.6%; symptoms of peripheral vascular disease in 4.8%, and 1.8% had amputations of the lower limb for gangrene. The prevalence of hypertension was 23%. Obesity was seen in 16% and central obesity in 21.3%. Forty per cent of males and 1.8% of females were smokers or ex-smokers. Eleven per cent had hypercholesterolaemia; 14% had hypertriglyceridaemia; 12% had low HDL cholesterol.

Urine albumin was >50 mg/l in 29%, and 2% had established chronic renal failure. A total of 15% had retinopathy on presentation. Sixteen percent had cataracts at examination, or gave a history of cataract extraction; if slit-lamp examination had been performed, this proportion would be considerably greater. One per cent were legally blind (visual acuity worse than 6/60).

The difference in prevalence of complications in symptomatic patients vs. in those detected at health screening was not statistically significant.

Discussion

Complications of diabetes have been thought to occur late in the course of the disease. However, type 2 diabetes (formerly called non-insulin-

dependent diabetes mellitus, NIDDM) is an insidious illness with a long preclinical asymptomatic phase. Patients may be exposed to the ill-effects of asymptomatic hyperglycaemia for many years before they are diagnosed. It is not surprising that patients with type 2 diabetes have evidence of diabetic tissue damage at the time of diagnosis.[19,34,35] In Finland, 1.5% of recently-diagnosed diabetic subjects had neuropathy with symptoms, 2.3% had neuropathy with signs.[18] In the UK, 5% had retinopathy and foot ulceration at diagnosis.[35] Data on the prevalence of complications at presentation in developing countries are scarce. Published data are based on studies in immigrant populations such as in the UK Prospective Diabetes Study (UKPDS) cohort.[19] Our study shows that a significant proportion of Sri Lankan patients with type 2 diabetes had complications at diagnosis.

The prevalences of coronary vascular disease, hypertension, stroke, neuropathy and retinopathy were all higher in our series than in the UKPDS Caucasian and Indo Asian recruits.[19] Peripheral vascular disease was less common in our patients.

In the UKPDS, those with severe cardiovascular and renal disease were excluded. The presence of such patients may explain the increased prevalence in our patients.

In developed countries, striking differences in the prevalence of nephropathy and macrovascular disease have been demonstrated in disadvantaged minority groups.[36] A higher prevalence of neuropathy with a shorter duration of type 2 diabetes has been reported in American Blacks and Hispanics.[36] While a genetic predisposition to develop complications cannot be discounted, exposure to a longer duration of asymptomatic hyperglycaemia due to poor access to adequate health-care facilities, due to lower socioeconomic status, may also be a contributory factor.[36] Hence both genetic factors and a paucity of health-care resources may contribute to this high prevalence of complications in newly-diagnosed patients with type 2 diabetes in Sri Lanka.

Macrovascular disease[8] and retinopathy[10] account for significant morbidity and mortality in Sri Lankan diabetic patients. Secondary prevention of complications by diabetes health-care teams can be cost-effective in a Sri Lankan setting.[12–15] Secondary prevention usually commences at diagnosis. When complications such as retinopathy and neuropathy have been found even at presentation in asymptomatic patients, this is too late. A population-based lifestyle modification programme for primary prevention of diabetes should be implemented.

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