Risk factors for long-term complications in patients with type 2 diabetes, in Sri Lanka.

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Abstract

Objective: To identify risk factors for long-term complications in patients with type 2 diabetes in Sri Lanka.

Methodology: An unmatched, clinic-based, case control study. Diabetic patients enrolled from randomly selected medical clinics from primary, secondary and tertiary care level hospitals were interviewed to determine possible risk factors and screened for long-term complications. 252 diabetic patients having one or more long term complications were selected as cases and 288 diabetic patients free from long term complications included as controls.

Results: Peripheral diabetic neuropathy (25.2%), micro albuminuria (22.8%), retinopathy (20%), and coronary heart disease (12.4%) were some complications present among cases. 21.9% had only one complication while 16.5% and 6.9% had two and three complications respectively. Only 1.5% had all four complications.

In the univariate analysis, smoking, low family income, body mass index over 25, older age (over 60 years), longer duration of diabetes (11-15 years), random blood sugar > 11.0mmol/l, raised diastolic blood pressure > 90mmHg were significantly ($p < 0.05$) associated with the development of long-term complications. The latter four factors were significantly associated with a number of complications. Multivariate analysis identified older age (OR = 5.51 CI 1.59, 19.17), duration of diabetes (OR = 2.08 CI 1.23, 3.50), random blood sugar 11.0-16.7 mmol/l (OR = 3.15 CI 1.31, 7.56) and current smoking (OR = 8.88, CI 1.53, 51.53) as significant risk factors.

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Conclusion: Long-term complications in type 2 diabetes are common among patients. Most of the significant risk factors are preventable.

Key Words: Type 2 diabetes, long-term complication, risk factors, clinic based

Introduction

The early detection and identification of the risk factors contributing to the development of long-term complications in diabetes is an important strategy to minimize the human suffering and costs of the conditions (1). There are several factors related to person characteristics, clinical variables and the delivery of care that play an important role in the development of complications (2). Most of these risk factors are considered as avoidable. Poor compliance, uncontrolled diet and lack of knowledge on disease are also associated with an increased risk of development of complications (2). Cigarette smoking is a well-established risk factor for the progression of diabetic complications, where as an association with alcohol consumption is not very clear (1,2). Type of diabetes, duration, glycaemic control and uncontrolled hypertension are the strongest clinical predictors of the outcome (3, 4).

Diabetes currently afflicts more individuals than some of the communicable diseases in Sri Lanka and it has now emerged as a major public health problem. The National Diabetic Association estimates that there are one million people with diabetes in Sri Lanka (5). Studies done in Sri Lanka have reported that long-term complications are an emerging problem in this country (6, 7).

There appear to be challenges in the management of diabetes and its complications in Sri Lanka viz. increasing prevalence, uncertainties in risk factors of diabetes complications in our settings, and limited health care facilities on screening and management of diabetes complications. Therefore, this study was undertaken to investigate the relationship of long-term complications with some selected risk factors amongst patients with type 2 diabetes.

Method

This was a clinic based cross sectional study, designed as an unmatched case control study. This study was carried out during the period of 1998-1999 in the Western Province of Sri Lanka. Primary, secondary and tertiary level government institutions with diabetic clinic facilities were

Table 1 : Univariate analysis

Socio-demographic Characters	Case (n=252)		Control (n=288)		Odds Ratio	C.I. at 95%
<i>Age</i>						
Below 40 yr.	5	1.9	24	8.4	1.00	
40 - 60 yr.	112	44.5	155	53.8	3.47	(1.24, 11.96)
Over 60 yr.	135	53.6	109	37.8	5.94	(2.12, 20.49)
<i>Income (Rs)</i>						
< 2500	126	50.0	112	38.9	1.00	
2500-5000	75	29.8	117	40.6	0.57	(0.38, 0.85)
> 5000	51	20.2	59	20.5	0.77	(0.48, 1.24)
<i>Continues treatment</i>						
Yes	195	77.4	232	80.6	1.00	
* No	57	22.6	56	19.4	1.21	(0.78, 1.87)
<i>Smoking</i>						
Non-Smokers	215	85.3	258	89.6	1.00	
Ex-smokers	13	5.2	22	7.6	0.71	(0.33, 1.51)
Current smokers	24	9.5	8	2.8	3.6	(1.50, 8.90)
<i>Alcohol</i>						
Non- alcoholic	219	86.9	242	87.5	1.00	
Ex-drinker	16	6.4	15	5.2	1.17	(0.56, 2.69)
Current drinker	17	6.8	21	7.3	0.89	(0.46, 1.90)
<i>Disease Duration</i>						
5 - 10 Years	196	77.8	248	86.1	1.00	
11- 15 years	35	13.9	23	7.9	1.93	(1.07, 3.49)
> 15 years	21	8.3	17	6.0	1.56	(0.77, 3.20)
<i>RBS (mmol/l)</i>						
<11.0	131	52.0	204	70.8	1.00	
11.0 - 16.7	90	35.7	58	20.1	2.42	(1.85, 7.90)
>16.7	31	13.3	26	9.1	1.86	(1.24, 6.86)
<i>Systolic BP (Hg mm)</i>						
<160	198	78.6	235	81.6	1.00	
160 or above	54	21.4	53	18.4	1.26	(0.80, 2.00)
<i>Diastolic BP (Hg mm)</i>						
<90	131	52.0	176	61.1	1.00	
90 or above	121	48.0	112	38.9	1.45	(1.02, 2.07)
<i>BMI</i>						
< 25	14	5.6	32	11.1	1.00	
25 - 27	143	56.7	151	52.4	2.16	(1.07, 4.57)
> 27	95	37.7	105	36.5	2.07	(1.00, 4.45)
<i>Cholesterol (mmol/l)</i>						
<6.2	172	68.4	202	70.2	1.00	
6.2 or more	80	31.6	86	29.8	0.92	(0.78, 4.48)

* No Treatment continuity - Off oral glucaemic treatment > 3 months, without medical advice

**Table 2: Logistic regression analysis. Outcome variable - long-term complication(s)
Vs none**

Variable	Coefficient	SE	P-value	Odds ratio	C. I. At 95%
Intercept	-2.74	0.99	0.01	0.64	0.01, 0.45
<i>Age</i>					
40-60 years	1.47	0.63	0.01*	4.35	1.27, 14.83
above 60 years	1.71	0.64	0.007*	5.51	1.59, 19.17
<i>Family Monthly Income</i>					
2500-5000 Rs	-1.09	0.34	0.01*	0.34	0.17, 0.66
Over 5000 Rs	-0.88	0.63	0.16	0.41	0.12, 1.41
<i>Duration</i>					
11 - 15 years	0.73	0.27	0.006*	2.08	1.23, 3.50
> 15 years	-0.98	0.52	0.99	0.99	0.36, 2.75
<i>RBS</i>					
11.0-16.7 mmol/l	1.147	0.45	0.01*	3.15	1.31, 7.56
above 16.7 mmol/l	0.1420	0.54	0.79	1.15	0.40, 3.29
<i>Smoking</i>					
Ex-Smoker	0.18	0.70	0.89	1.19	0.30, 4.73
Current Smoker	2.18	0.99	0.01*	8.88	1.53, 51.53
Deviance on 513 d.f. = 546.46 * P< 0.05 ** P< 0.01					

Reference categories: Age <40 years, Monthly Family Income less than 2500 Rs Duration < 10 years, RBS < 11.0 mmol/l, Non-Smoker

selected as study centres using the simple random sampling method.

A case was defined as a patient attending clinic and diagnosed as type 2 diabetes for a period of 5 years and newly identified with one or more of the following long-term complications during the survey: diabetic retinopathy (by direct ophthalmoscopy after pupillary dilation and the presence of microaneurysms, haemorrhages, cotton wool spots, microvascular abnormalities. Exudates were not considered, because they were not specific for diabetes.) (8); peripheral diabetic neuropathy (the insensitivity to the 5.07g monofilament at one or more of nine sites on either foot) (9); diabetic nephropathy (presence of microalbuminuria, 20 to 200 mg/l, in two consecutive urine collections) (10); Coronary heart diseases (based on ECG records: coronary probable, coronary possible and normal, according to Minnesota coding system) (11).

Controls were patients attending the diabetic clinic and diagnosed as type 2 diabetes for a period of 5 years, but free from long-term complications at the time of screening.

Patients, who were diagnosed as type 2 diabetes, within last five years and were under treatment or treated for the complications or/and risk factors being studied, as well as pregnant women and those who did not co-operate for any reason were excluded.

The sample size was calculated with sufficient power (90%) to detect effects with a 95% confidence interval. Selection of cases and controls was done by enrolling all consecutive cases and controls screened from the eligible diabetic patients. This sample size included 10% guard against non-response and 30% for confounding variables.

At the preliminary stage nearly 700 eligible subjects were identified. They were invited to a special screening clinic and 570 responded. Following the screening, 252 respondents were identified as cases and 288 as controls. World Health Organization (WHO) recommended guidance was used to check the blood pressure (BP). A standard mercury sphygmomanometer was used with a 23 x 14cm cuff (bladder 23 x 13cm) and a larger cuff for obese patients. Precision- G Glucometer/ Medi Sense-2 blood glucose test strips were used to detect random blood sugar

(RBS) and Micral Test II strips to test urine microalbuminuria (MA). Twelve lead resting electrocardiograms (ECG) were taken and coded by the Minnesota codes (11). The patient's clinic records were also used to abstract the information on patient's disease status. The patients were interviewed to obtain relevant information for the study.

Preliminary univariate analysis identified that many factors are significantly associated with the risk of long-term complications. Since the long-term complications have many possible outcome variables and the study design was an un-matched case control study, a logistic regression model was used (EGRET software) with the forward selection procedure.

Results

Peripheral diabetic neuropathy (25.2%) was the commonest complication among the study population, whereas the coronary heart disease (12.4%) was the least common. Diabetic retinopathy and diabetic nephropathy / MA were 20.0% and 22.8% respectively. 21.9% had one complication, while only 1.5% had all the complications. 16.5% and 6.9% respectively had two and three complications.

Person factors

Elderly age and lower monthly family income were statistically significant ($P < 0.05$) socio-demographic characters associated with the development of long-term complications, (Table 1). Older age of over 60 years had nearly a six fold increased risk. The patients who had discontinued treatment also had greater risk of developing long term complications.

Smoking ($p < 0.01$) was the only other significant person risk factors found in the present study. A 3.6 fold increased risk of long-term complications was seen among current smokers. The mean duration of diabetes and amount of smoking between current and ex-smokers were also assessed. Both mean duration and amount smoked for current smokers were significantly ($p < 0.001$) higher for cases than for the controls. However, the difference with mean smoking duration and the difference with the mean number of cigarettes/day of ex smokers among cases and controls were not statistically significant ($p > 0.05$).

Clinical variables

The risk of development of long-term complications increased with the duration of diabetes (Table 1 & 2) up to 15 years. Beyond 15 years this risk decreased with longer duration. High RBS level over 11mmol/l was significantly

($p < 0.01$) associated with the development of long-term complications (Table 1 & 2). A three times increased risk of developing long-term complications for subjects with random blood sugar level of 11.0-16.7mmol/l was observed. When the RBS level was more than 16.7mmol/l, this risk was reduced. However at higher level of RBS (> 16.7 mmol/dl), they had more significant ($p < 0.005$) tendency to have more number of complications.

Arterial hypertension was defined according to the ADA and WHO criteria: systolic BP > 160 mm Hg or diastolic BP > 90 mm Hg (12). The mean systolic BP for cases and controls was 142.4mmHg and 139.7 mmHg respectively, while the mean diastolic BP among cases and controls were respectively 86.7mmHg and 84.8mmHg. Both high systolic and high diastolic BP are associated with a higher risk of developing long-term complications (2,4). In this study however only raised diastolic blood pressure was statistically significant ($p = 0.03$). Neither systolic ($p = 0.75$) nor diastolic ($p = 0.61$) blood pressures was statistically significantly associated with the number of complications in type 2 diabetes.

There is a twofold increase in the risk of complications when body mass index (BMI) is more than 25. The level of serum cholesterol was statistically not significantly ($P > 0.05$) associated with complications in type 2 diabetes. The patients with high level of serum cholesterol (> 6.2 mmol/l) was at a lower risk, compared to the lower serum cholesterol of less than 6.2 mmol/l. There was no statistically significant association ($P > 0.05$) between the level of serum cholesterol and the number of long-term complications.

Discussion

Diabetes, once thought to be a disease of affluent countries, has emerged as a public health concern in the developing countries, including Sri Lanka. The age adjusted (30 -65 years) crude prevalence of diabetes for the adult population in Sri Lanka is around 5% (5). In Sri Lanka, patients are able to visit any government health facility they chose. The majority of the study population was female, above the age of 40 years, and from low income groups. This is expected as the majority of working men with diabetes are likely to receive their diabetes care privately.

Thus the findings of this study are generalisable to the patients receiving care in government clinics, but may not apply to those receiving private care. This was one of the limitations in the present study.

Person related risk factors

As reported in earlier studies in many parts of the world, this study also identified that persons of older age over 60 years and low income groups are at higher risk for the development of long-term complications (2, 13). Increased risk of developing long-term complications at an older age is inevitable, because early onset of diabetes leads to a longer duration of the illness. Even after controlling for these confounding effects, age was a highly significant risk factor in developing long-term complications in type 2 diabetes.

Continuity of treatment is an important factor in controlling or preventing any disease. This may be affected by many other factors such as, severity of the disease, remissions, use of other traditional methods, ignorance etc. This study identified that discontinuity of treatment had a higher risk of developing long-term complications. Studies done in Sri Lanka and abroad had reported the importance in continuity of treatment in the prevention and control of complications in diabetes and therefore the importance of continuous

treatment should be highlighted in the management of long-term complications (6, 13, 14).

Effects of smoking on diabetes and long-term complications are well known and established (1, 2). This study too revealed similar findings. It was interesting to note, that heavy smokers had a relatively lower risk than average smokers. The possible reason is survival of average smokers than the heavy smokers. In this study, the inverse association between alcohol consumption and long-term complications was established. Orchard et al described, that there was no evidence of long-term alcohol intake and dose response relationship in developing long-term complications. In fact they revealed an inverse relationship between alcohol and glycaemia (13). Both smoking and alcohol are predominantly seen in males in Sri Lanka. In this study females accounted for 80% of the study population. As only a small number of males were included, the results should be interpreted with caution.

Clinical risk factors

Duration of diabetes, poor GC, raised BP, high level of cholesterol and BMI are established risk factors for complications of diabetes (2, 4, 6, 13). This study also revealed similar findings except in cholesterol: two fold increased risk with long duration of diabetes (11-15 years) and higher RBS over 11.0 mmol/l and, BMI over 25. Also all these were statistically significant ($p < 0.01$). Although, the patients with recorded high systolic (>160 mm Hg) and high diastolic (>90 mm Hg) blood pressure were found to be at higher risk of developing long-term complications, it was observed that only raised diastolic blood pressure was significant as a risk factor for diabetic complications. Other studies have reported possible risk of either one or both systolic and diastolic blood pressure in complications of diabetes (4,15,16).

However interestingly, longer duration of diabetes (over 20 years), very high level of RBS (>16.7 mmol/l), raised cholesterol (>6.2 mmol/l) and high BMI (>27) showed a decreasing trend of risk in the present study, which is contrary to the findings of the studies carried out in other countries (3, 13). The observed lower risk of complications in those with longer duration of diabetes, very high level of RBS is probably a function of a relative survival.

The two major limitations in this study were; (i) non-use of more advance techniques to screen some diabetic complications (HbAs for glycaemic control and Neurothesiometer to detect diabetic neuropathy), these may cause some misclassification of disease status (ii) risk factors were studied for all complications together, but not separately for each complication. Using more advanced techniques in screening and studying a large sample for each complication would have been ideal, but could not be carried out due to practical and other logistic constraints.

In conclusion, our findings suggest that long-term complications in type 2 diabetes are important health problems among patients attending state sector clinics in Sri Lanka. Most of the identified risk factors are preventable. It is obvious with the increase of incidence and prevalence of diabetes, long-term complications of diabetes will tend to rise. Hence, strategy will be plan and implement 'risk factors' oriented preventive

programmes. Widespread coverage of basic investigation facilities and centres of excellence with advanced techniques for diagnosis of long-term complications should also be established. Further studies are needed in the field of epidemiology of long-term complications of diabetes.

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