ORIGINAL ARTICLE

Proteinuria in Diabetic Patients in a Primary Health Care Setting in Sarawak

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Summary

Diabetic nephropathy is now the number one cause of end stage renal failure in Malaysia. This places a huge burden on patients and the health care system especially in developing countries with limited health care resources, such as in Sarawak in East Malaysia. This study describes the prevalence of proteinuria/microalbuminuria in diabetic patients treated in Klinik Kesihatan Tanah Puteh. Early detection of proteinuria/microalbuminuria allows remedial measures to be taken to retard the progression of nephropathy. Forty-eight percent of the cases had proteinuria and microalbuminuria was found in 16%. Seventy-eight percent of cases with proteinuria were on treatment with angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers. Seventy-five percent of patients had hypertension but only 6% achieved the targeted BP of <130/80 mmHg.

Key Words: Diabetic nephropathy, Proteinuria, Microalbuminuria, Primary health care, Sarawak, Malaysia

Introduction

Diabetes is a major cause of end-stage renal failure (ESRF) in many countries in the world including Malaysia. In the year 2002, 47% of new cases of ESRF starting dialysis were due to diabetic nephropathy[1]. Risk factors for the development of diabetic nephropathy include poor glycaemic control, hypertension and smoking. Early detection, aggressive intervention of risk factors and the use of angiotensin-converting-enzyme inhibitors (ACEi) and angiotensin-receptor blockers (ARBs) have been shown to retard the progression of diabetic nephropathy[2].

There is no reported study on diabetic nephropathy in a primary health care setting in Sarawak. This study examined the prevalence of microalbuminuria, overt proteinuria and hypertension in diabetic patients. It also looked at the control of blood pressure and the use of ACEi/ARBs in these patients.

Klinik Kesihatan Tanah Puteh (KK Tanah Puteh) is a primary health care clinic serving the urban population of the city of Kuching, the capital of Sarawak in East Malaysia. The KK Tanah Puteh has a diabetes unit, managed by a nurse educator and a medical assistant with the help of the medical officers in the clinic.

The earliest clinical manifestation of diabetic nephropathy is microalbuminuria. This may progress to overt proteinuria if untreated over a period of 7 to 10 years and may eventually result in ESRF[3]. Studies have shown that the onset and course of diabetic nephropathy can be ameliorated significantly by several interventions especially if these are instituted early in the course of the disease[4].

Several studies have shown that intensive glycaemic control reduces the risk of development of diabetic microvascular complications including the development of nephropathy[5,6]. Tight blood pressure (BP) control has

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also been shown to slow the progression of nephropathy[7]. Use of agents that block the rennin-angiotensin system has been shown in recent clinical trials to retard the progression of diabetic nephropathy[8,9,10].

Materials and Methods

This is a cross-sectional study investigating the profile of diabetes control and renal function of the diabetic patients registered in the diabetic clinic of KK Tanah Puteh. The study was conducted from January to March 2003. The diagnosis of diabetes mellitus was made according to the blood sugar values proposed by the WHO diagnostic criteria[11]. The target for control of diabetes mellitus was based on the recommendation by the International Diabetic Federation (IDF, Europe)[12]. The diabetic patients were managed according to the Malaysian national guidelines for diabetes, hypertension and hyperlipidaemia[13,14,15].

Information on patient demography, type of diabetes, cardiovascular risk factors (BP, lipids, BMI and smoking history), glycaemic control (HbA1c and FBS), renal function (serum creatinine, microalbuminuria and proteinuria) and treatment rendered (pharmacological and non pharmacological) were collected from the clinic cards. All available data were tabulated and descriptive statistical analysis was performed.

Patients attending the diabetes clinic had at least a urine test done every year. A random urine sample was tested for proteinuria using Bayer Labstix® reagent strips. Patients with a negative test were then tested for microalbuminuria. Microalbuminuria was calculated using the albumin-to-creatinine ratio in a random spot urine collection. This is a quantitative test for microalbumin with a sensitivity ranging from 56% to 100% and specificity from 81% to 98%[16].

Blood pressure (BP) achieved was grouped according to the treatment targets by IDF. Optimal blood pressure was defined as BP <130/80 mmHg, fair control as BP 130-140/80-90 mmHg and poor control as BP >140/90 mmHg.

Results

There were 1337 cases registered in the diabetic registry as at 31st December 2002. Cases which had defaulted, died or was transferred to another clinic were excluded from the study. Data of the remaining 1031 cases were examined and 970 cases had results of urine tests for analysis. The full demography of the study population has been described elsewhere[17]. Women outnumbered men by a ratio of 63:37. Ninety-eight percent (98%) of the cases had type 2 diabetes. The patient's age ranged between 24 and 92 years with a mean of 59±12 years.

The patients had their urine tested annually. In the 970 cases where urine test results were available 315 (32%) tested positive for proteinuria using urine dipstick. Seventy-three percent of the cases who tested negative for proteinuria (476 cases) were further tested for microalbuminuria. Out of the 476 case 155 (32%) had a positive test for microalbuminuria. This was based on a single test for microalbumin.

Hence, of the 970 patients with urine tested, 470 cases (48%) had proteinuria or microalbuminuria. Table I shows the distribution of the various degree of proteinuria. One hundred and fifty-five cases (33%) had microalbuminuria, 140 cases (30%) had trace proteinuria, 90 cases (19%) had urine protein 1+, 60 cases (13%) had urine protein 2+ and 25 cases (5%) had urine protein 3+.

The majority, 78% (365) of the patients with proteinuria/microalbuminuria were on treatment with either ACE-inhibitors or Angiotensin Receptor Blockers (ARB's). Of the 104 cases not treated with ACEi/ARB's, 10 cases had a raised serum creatinine level of >134umol/l and the reason for the remaining 93 cases were not clear. One case with proteinuria had no record of treatment.

Out of the 155 cases with microalbuminuria, 21% were already receiving either ACE-inhibitors or ARBs before the urine was tested. Sixty-one percent were started on ACEi/ARBs after the result of urine test was known. The remaining 18% were not put on these medications.

The majority of the patients, 725 out of 970 (75%) had a diagnosis of hypertension. The mean systolic BP was 137±17 mmHg whilst the mean diastolic BP was 85±10 mmHg. The distribution of blood pressure control is shown in Figure 1. There were more patients with proteinuria with a BP >140/90 mmHg than patients without proteinuria. Thirty-nine percent of the 470 cases with proteinuria/microalbuminuria had a BP> 140/90 mmHg whilst 31% of the 500 cases without proteinuria had high BP. This was statistically significant ($x^2 = 7.642$, df=2, p=0.022).

Among the hypertensive patients, 388 cases (53%) had proteinuria/microalbuminuria and 337 cases (47%) had no proteinuria. On average, 2 antihypertensive agents were used and 34% were on monotherapy. Optimal blood pressure of <130/80 mmHg was achieved in only 6% of patients.

Eighty-four percent of patients having both hypertension and proteinuria received either an ACEi or ARBs for treatment. ACEi was used in 98% of cases. However, only 51% of the patients who were normotensive but with proteinuria/microalbuminuria received treatment with either ACEi or ARBs. Overall the use of ACEi/ARBs was common and they were used in 55% of the 970 cases studied.

There were 225 patients who had diabetes for > 10 years and 54% of these patients had proteinuria/microalbuminuria. Five-hundred and fifty patients had diabetes for < 5 years and 46% of these had proteinuria. Although the patients diagnosed with diabetes for a longer duration were more likely to have proteinuria, it did not reach statistical significance (p=0.059).

Table I: Distribution of proteinuria in relation to treatment with ACE inhibitors or angiotensin blockers

Urinary protein level (n= 970)	Treatment		No treatment	
	%	(n)	%	(n)
No proteinuria a	52.5	(94)	47.5	(85)
Microalbumin negative	73.8	(237)	26.1	(84)
Microalbumin positive	17.4	(27)	82.6	(128)
Proteinuria trace (<300mg/l)	32.9	(46)	67.1	(94)
Proteinuria 1+ (>300mg/l)	15.6	(14)	84.4	(76)
Proteinuria 2+ (>1g/l)	21.7	(13)	78.3	(47)
Proteinuria 3+ (>3g/l)	16.0	(4)	84.0	(21)
Proteinuria 4+ (>20g/l)	0.0	(0)	0.0	(0)

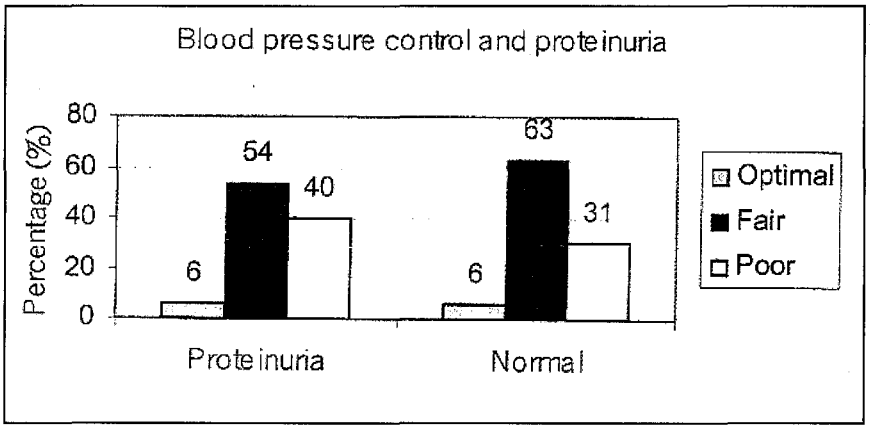

Fig. 1: The distribution of achieved blood pressure control

Discussion

This study shows that 48% of diabetic patients treated at KK Tanah Puteh had some degree of proteinuria/microalbuminuria and 78% of these cases were on treatment with either an ACEi or ARB. One third (32%) of the patients who tested negative for urine protein by dipstick, had tested positive for microalbuminuria. Microalbuminuria denotes the earliest clinical stage of diabetic nephropathy and it is potentially reversible with intervention. Besides indicating incipient diabetic nephropathy, it is also a marker of increased cardiovascular risk[18]. It is important to note that in this study population, 33% of 470 the patients with proteinuria had microalbuminuria on one occasion. This needs to be repeated as several factors such as uncontrolled diabetes, hypertension or urinary tract infection can affect albumin excretion in the urine[4]. Nevertheless, it is likely that a significant number of patients really have persistent microalbuminuria and would benefit from intervention.

From this study, only 21% of the group of patients with microalbuminuria were on pre-existing ACEi/ARBs but another 61% were started on treatment after the urine microalbumin status was known. By testing for microalbuminuria, the proportion of cases receiving ACEi/ARBs had increased from 21% to 83%.

Tight BP control has been shown to be very important in slowing the progression of diabetic nephropathy especially when the patient already has overt proteinuria. It is recommended that the optimal BP should be <130/80mmHg and for those with proteinuria >1gram/day, BP should be further reduced to 125/75 mmHg[8,19].

However, this is difficult and often not achieved as evident in this study. Only 6% of the patients had BP of <130/80 mmHg. To achieve the target BP, multiple agents are often needed[20]. Patients in the study were on an average of 2 anti-hypertension medications. However, patients given more anti-hypertensive did not achieve better control than those on monotherapy. This may mean more severe disease or poorer patient compliance. Greater emphasis needs to be placed on BP control in the future management of these patients. ACEi and ARBs are the anti-hypertensive of choice[2,4,13,14]. The majority of patients were on ACEi because they are cheaper and more readily available in the polyclinic setting. Only those who cannot tolerate ACEi were switched to ARBs and this happened in 2% of the patients.

Conclusion

Diabetic nephropathy has become a major cause of morbidity and mortality in our country. Screening for proteinuria and microalbuminuria can be easily performed in a primary health care setting. This can pick up patients at risk for developing ESRF and cardiovascular disease. These patients will benefit from aggressive control of their glycaemia and blood pressure with the use of ACEi/ARBs. As shown in this study, optimal BP control is often difficult to achieve and special attention needs to be focused on this.

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