

ORIGINAL ARTICLE

RISK FACTORS FOR DIABETIC NEPHROPATHY AMONG NON INSULIN DEPENDENT PATIENTS WHO ATTENDED CITY HALL'S STAFF CLINIC IN KUALA LUMPUR

Umi Ahmad, Md. Idris Mohd Nor & Osman Ali

ABSTRACT

Diabetes mellitus and its main complication, nephropathy, affects the economic wellbeing and quality of life of the sufferers and the population. A matched case control study was conducted in September 1998 to investigate the factors involved with nephropathy such as diabetic control, smoking, hypertension, family history of diabetes and diabetic duration. Respondents were classified based on the presence of microalbuminuria or macroalbuminuria. Seventy-two pairs of case and control were studied. Duration of diabetes ($p = 0.005$), presence of lethargy and weakness prior to diabetes diagnosis ($p = 0.019$), duration of smoking ($p = 0.014$), duration of hypertension ($p = 0.000$), systolic hypertension ($p = 0.025$), uncontrolled diabetes with poor HbA1c level ($p = 0.026$) and lack of diabetes knowledge ($p = 0.037$) were factors which related significantly to nephropathy by univariate analysis. In multivariate analysis, systolic hypertension ($p = 0.0015$), lack of diabetes knowledge ($p = 0.0197$), presence of lethargy symptom ($p = 0.0027$), prolonged diabetic duration ($p = 0.0301$) and higher body mass indices ($p = 0.0213$) were predictors to diabetic nephropathy.

Key words: Diabetes mellitus (NIDDM), nephropathy, risk factors.

INTRODUCTION

Diabetes mellitus (NIDDM) has become a major chronic non-communicable disease in the world including Malaysia. Its complications of macrovascular and microvascular might affect the quality of life of the patients and their dependents. Previous study showed that the cumulative incidence of the albuminuria excretions amongst NIDDM was 17% after having the diabetes for five years. This incidence will increase to 37% after 10 years and 67% after 15 years¹. The presence of microalbuminuria can become a predictor to mortality due to cardiovascular complications^{2,3}. It has been used to estimate the rate of kidney failure amongst the NIDDM patient but for IDDM patient, it has been used as a prognostic factor to predict the kidney failure in the next 15-20 years⁴.

Hyperglycemia was known to aggravate albuminuria amongst NIDDM. It was found that the increased in the level of HbA1c will influenced the proteinuria^{5,6}. However, it was shown that smoking among the diabetics will also influence the albuminuria and it correlated well with the number of cigarettes⁷. It was believed that smoking activates the clinical proteinuria⁸ however, Gall et al (1997) disagree that smoking influenced nephropathy among diabetic patients. Hypertension on the other

hand, was found as a promoter to the nephropathy. Among the IDDM, it was found that the nephropathy occurs after 10 years of diabetic⁹.

The objective of this study was to determine the risk factors for nephropathy among diabetics (NIDDM) attending staff clinic of City Hall, Kuala Lumpur.

MATERIALS AND METHODS

The pair-matched case control study was conducted among staffs clinic of City Hall, Kuala Lumpur in September 1998. A total of 72 pairs of cases and were selected, matched by age and sex. The NIDDM patients were randomly chosen from the attendance list and HbA1c test was carried out. They were instructed to collect their early morning urine to determine the presence of albuminuria. Urinestix strip was used to determine the microalbuminuria and microalbumin-kit for the microalbuminuria). Patients with total albumin levels exceeding 40 µg/ml was selected as case whilst the normal deemed as a control. Urine full examination and microscopic examination (UFEME) test was then carried out among cases to exclude albuminuria due to urinary infection. Patients having urinary infection, IDDM, hematuria, congestive heart disease, past history of glomerulonephritis and kidney cancer were excluded from the study.

The data was obtained from interviews using pretested questionnaire and from patient's medical record. The blood pressure measurements were measured by using sphygmomanometer. The degree

¹ Department of Community Health, Faculty of Medicine, UKM, Jalan Yaacob Latiff, Bandar Tun Razak, Cheras, Kuala Lumpur

of diabetic control was measured by using HbA1c levels, which was tested in private laboratory and patients who exceeded 8%, was considered having uncontrolled diabetes (DCCT Research Group, 1993). Body mass index (BMI) was calculated by using formula of weight (kg)/ height (m²). Females having BMI of more than 26 kg/m² and male of more than 27 kg/m² were classified as overweight. Smokers were defined as patients who smoked more than 10 packs/year and ex-smokers were patients who smoke before but has quit recently. The knowledge on the diet was measured by using series of questions and those who scored 32 out of 40 marks were considered knowledgeable.

Statistical analysis was carried out by using the SPSS program. For dichotomous variables, the Mc Nemar χ^2 test were carried out. Paired t-test was used to analyze quantitative variables. Logistic regression test was used to assess multiple risk factors.

RESULTS

Sociodemography

Out of 72 pairs, 54 pairs (75%) were males and 18 (25%) were females. Table 1 shows the characteristics of the cases and controls. There was no significant difference between cases and controls in term of racial distribution, educational level, marital status and monthly income.

Duration of Diabetes Mellitus

Cases have longer duration of diabetes illness as compared to control group. The mean duration among cases was 79.5 ± 58.0 months as compared to 56.5 ± 48.8 months among controls (paired t-test = 2.868, p = 0.005). The odds ratio for developing nephropathy among patients who have had diabetes for 5 years or more was 3 (95% confidence interval 1.33-6.76). It was found also that the duration of diabetes was significantly correlated with blood glucose levels (r = 0.216, p = 0.009).

Table 1: Characteristics of cases and controls

Descriptions	Cases (%) n=72	controls (%) n=72	χ^2 / paired-t test	df	p
Race					
Malays	51 (70.8%)	41 (56.9%)	$\chi^2 = 3.951$	1	0.413
Non Malays	21 (29.2%)	31 (43.1%)			
Age (min years)	47.14 ± 5.63	46.78 ± 5.55	Paired t test = 1.658	71	0.102
Education level					
Not schooling	4 (5.6%)	1 (2.8%)	$\chi^2 = 7.748$	3	0.560
Primary school	32 (44.4%)	34 (47.2%)			
Secondary school	35 (48.6%)	33 (45.8%)			
University	1 (1.4%)	3 (4.4%)			
Income	927.28 ± 647.88	1008.60 ± 607.01	Paired t test = 0.904	71	0.365
Marital status					
Married	67 (93.0%)	66 (91.7%)	$\chi^2 = 17.243$	2	0.008*
Widow	2 (2.8%)	2 (2.8%)			
Bachelor	3 (4.2%)	3 (5.5%)			

Significant at p < 0.05

Diabetes symptoms

Polyuria was the main symptom amongst the cases and controls but there was no significant difference between the two groups. Symptom of lethargy before being diagnosed as diabetic was found to be a

significant symptom associated with diabetic nephropathy where $\chi^2_{MN} = 5.26$, p = 0.019 (Table 2). There were no other significant differences in diabetic symptom for the two groups.

Table 2: Diabetic symptoms amongst cases and controls

Symptoms	Cases (%)	Control (%)	χ^2_{MN} # (n=71 pairs)	P
Polyuria	57(79.2)	50 (70.4)	1.71	0.189
Polydipsia	52(72.7)	47 (66.2)	0.552	0.458
Lethargy	19(26.4)	8 (11.3)	5.26	0.019*
Loosing weight	15(20.8)	16 (22.5)	0	1.000

* Significant at $p < 0.05$ # a control did not response

Smoking

There was a significant difference in the duration of smoking among the cases as compared to the controls of which the duration of smoking among cases was longer than the controls. However, there was no significant difference between cases and control in the number of cigarettes and packets of cigarettes/year smoked (Table 3).

57 months as compared to 60 ± 56 months among controls (paired t-test = 5.430, $p < 0.05$). There was a significant relationship between systolic hypertension and diabetic nephropathy where $\chi^2_{MN} = 4.32$, $p = 0.038$, however no similar result was found for diastolic hypertension (Table 4).

Hypertension

There were 32 cases (44.4%) and 23 controls (31.9%) giving history of hypertension. The duration of hypertension among the cases was $148 \pm$

Diabetic control and obesity

There was a significant relationship between HbA1c levels and nephropathy where $\chi^2_{MN} = 4.97$, $p = 0.026$. However, the body mass index (BMI) did not seem to influence nephropathy ($\chi^2_{MN} = 0.026$, $p = 0.871$) (Table 5).

Table 3: Distribution of smoker among cases and controls

Categories	Cases(n=72)	Controls(n=72)	χ^2_{MN} / paired t-test	P
Smoker	16 (22.2%)	21 (29.2%)	$\chi^2_{MN} = 0.84$	0.359
Ex-smoker	15 (20.8%)	15 (20.8%)	$\chi^2_{MN} = 0$	1.000
Mean duration smoking (months)	246.00 ± 82.43	173.62 ± 89.63	Paired t = 2.688	0.014*
Min cigarettes per day (stick)	15.81 ± 8.5	18.10 ± 14.4	Paired t = -0.523	0.607
Smoking < 10 packs/year and non smoker	49 (68.1)	55 (76.4)	$\chi^2_{MN} = 1.136$	0.286
Smoking \geq 10 packs/year	23 (31.9)	17(23.6)		

*Significant at $p < 0.05$

Table 4: Distribution of hypertension and treatment among case and control

Categories	Cases (n=72)	Control (n=72)	χ^2_{MN} / paired t-test	P
Hypertension	32 (44.4%)	23 (31.9%)	$\chi^2_{MN}=2.06$	0.151
Min duration of hypertension	148 months	60 months	Paired t =5.430	0.000*
Diastolic hypertension	22 persons	18 persons	$\chi^2_{MN}=3.56$	0.059
Systolic hypertension	23 persons	11 persons	$\chi^2_{MN}=4.32$	0.025*

* Significant at p < 0.05

Table 5: Distribution of HbA1c and obesity

Categories	Case (%) n=72	control (%) n=72	χ^2_{MN}	P
HbA1c level				
Good	17 (23.6)	30 (41.7)	4.97	0.026*
Poor (>8%)	55 (76.4)	42 (58.3)		
Nutritional status				
Normal	30 (41.7)	32 (44.4)	0.026	0.871
obese	42 (58.3)	40 (55.6)		

* significant at p < 0.05

Factors associated with diabetic control

The factors that influenced the diabetic controlled were investigated by using HbA1c levels. When the diabetic controlled is poor, the risk of developing nephropathy will be high. Some of factors associated with poor diabetic control are poor compliance to the diabetic treatment, poor compliance to follow up and lack of knowledge in dietary control. In this study, the knowledge on diet was found to be a significant factor associated with nephropathy. The analysis has shown that 43.1% of cases were lacked

of knowledge compared to controls (25.0%) where $\chi^2_{MN}=4.36$, p = 0.037.

Logistic regression analysis was conducted to predict the development of nephropathy. All factors significantly associated with nephropathy in univariate analysis was included in the logistic model. In this study, systolic hypertension, lack of dietary knowledge, feeling lethargy prior to diabetes diagnosis, high body mass index and long duration diabetic contributed significantly to risk of diabetic nephropathy (Table 6).

Table 6: Logistic regression model to predict diabetic nephropathy

Variables	Regression coefficient (β)	Standard error	p	OR	CI (95%)
Constant	-4.7978	1.4618	0.0010*		
Systolic hypertension	1.3362	0.4204	0.0015*	3.80	1.67 - 8.67
Lack of diet knowledge	1.0216	0.4380	0.0197*	2.78	1.18 - 6.55
Lethargy symptom	1.6666	0.5563	0.0027*	5.29	1.78 - 15.75
Body mass index	0.0989	0.0430	0.0213*	1.10	1.01 - 1.20
Duration of diabetes	0.0084	0.0039	0.0301*	1.01	1.01 - 1.02

* Significant at p < 0.05

The model was developed from the logistic regression analysis;

Odd of diabetes nephropathy = EXP [-4.7978 + 0.0084 duration of diabetes + 0.0989 body mass index + 1.6666 lethargy symptom + 1.3362 systolic hypertension + 1.0216 poor dietary knowledge]

Attribute risk percent (ARP) and population attributable risk percent (PARP)

Attribute risk is a risk difference between the exposed individual and non-exposed individual. This risk comparison depicted the risk due to exposure to the risk factor whilst PARP is the proportion of nephropathy cases in the target population related to the presence of risk factors. (Table 7)

Table 7 shows that after adjusting for the other factors, about 73% of the diabetic nephropathy complication was attributed to systolic hypertension, 0.9% to diabetic durations, 81% to lethargy symptom prior diabetes diagnoses, 64% to poor dietary knowledge and 9% to increase of body mass index.

Table 7: Attributable risk percent and population attributable risk percent to diabetic nephropathy

Risk factors	Proportion of expose population (%)	ARP (%)	CI (95%)	PARP (%)	CI (95%)
Systolic hypertension	29.2	73.3	67 - 81	45.0	37 - 53
Duration of diabetes	33.3	0.9	-0.2 - 2.4	0.2	-0.5 - 1.0
Presence of lethargy	11.0	81.1	74.7 - 87.5	32.6	25.0 - 40.3
Poor diet knowledge	25.0	64.0	56.2 - 71.8	30.8	23.2 - 38.3
Body mass index	56.0	9.4	4.6 - 14.2	5.5	1.7 - 9.2

DISCUSSION

Diabetic nephropathy is one of the complication of diabetes mellitus. It occurs more often and in much shorter period in NIDDM as compared to IDDM. The presence of microalbuminuria is the earlier sign of nephropathy, it indicates the possibility of the patient to develop the cardiovascular complication more than the kidney failure. Therefore, the NIDDM patients have higher risk of heart attack in the presence of microalbuminuria. This is difference from the IDDM patient, which is more towards developing the kidney failure with a presence of microalbuminuria⁸.

In this study, it was found that patients with nephropathy have longer diabetic history as compared to the controls. Patient with a longer diabetic duration (≥ 5 years) has 3 times the risk of developing nephropathy complication as compared to the patients with shorter history of diabetes. The similar finding was reported in other studies^{1,5}. Duration of diabetes was positively correlated with blood glucose levels of which the blood glucose levels (indicating diabetes control) increased with the increased in the duration of diabetes. These explained the relationship between duration of diabetes and the nephropathy.

It was also shown that duration of smoking was significantly longer among the cases as compared to the controls. However, the difference

was not significant after controlling for other factors using logistic regression test. A similar result was reported by Gall et al. (1997)⁹, however, Klein et al. (1995)³ has found the reverse, but in his study the total pack/ years used was much higher.

The risk of nephropathy among patients with systolic hypertension was 3 times compared to patients without hypertension but relationship was not found for the diastolic hypertension ($p = 0.523$). The findings were found inconsistent in the literature, some studies produced the same results as this one^{5,10,11} but others like Powrie et al. (1994)¹², the finding was different. The different in characteristics of samples as well as degree of albuminuria could possibly explained the inconsistency.

This study found that HbA1c level of $> 8\%$ that indicates poor diabetic control was higher among the cases compared to the controls, $\chi^2 = 4.96$, $p = 0.026$. OR = 2.63 (CI_{95%} 1.12 - 6.16). Similar results were found in other studies^{5,9}. The diabetic control is influenced by various factors, however in this study only poor compliance towards diabetic treatment, less compliance to diabetic follow-up and poor knowledge on diabetic diet were studied. It was found by using multivariate analysis that poor knowledge on diet has a significant association with nephropathy after controlling the other factors. Other than that systolic hypertension, feeling of lethargy, obesity and duration of diabetic were also found a

significant predictors for a nephropathy in the logistic regression model.

The importance identifying factors associated with the development of nephropathy was to be able to prevent the complication from setting in. It can also be use to set priority for effective utilisation of resources. From this study, findings indicated that the intervention by reducing systolic hypertension and increasing patient's knowledge on diet will give a tremendous impact around 45% and 31% respectively to the prevalence of diabetic nephropathy in the population. Furthermore, the presence of lethargy prior to diabetic diagnoses could be used as a warning sign for the development of diabetic nephropathy among NIDDM patient, hence steps can be taken to avoid patients from developing premature nephropathy or even subsequent mortality.

CONCLUSION

Systolic hypertension, lethargy prior to diabetic diagnoses and lack of diabetic dietary knowledge are factors that can predict the development of diabetic nephropathy. Therefore, any programme performed to reduce the magnitude of diabetic nephropathy should focused on hypertension control and increased the patient knowledge on diabetic diet.

REFERENCES

- Nelson RG, Knowler WC, Pettitt DJ, Hanson RL, Bennett PH. Incidence and determinant of elevated urinary albumin excretion in Pima Indians with NIDDM. *Diabetes care* 1995; 18 (2): 182-187.
- Mattock MB, Morrish N, Viberti G, Keen H, Fitzgerald AP, Jackson G. Prospective study of microalbuminuria as predictor of mortality in NIDDM. *Diabetes* 1992; 41: 736-741
- Damsgaard EM, Froland A., Jorgensen OD, Mogensen CE. Eight to nine year mortality in known NIDDM and controls. *Kidney International* 1992 ; 41: 731-735
- DeFronzo RA. Diabetic Nephropathy. In Junior DP & Sherwin RS. (eds). *Diabetes Mellitus* 1997. Connecticut: Appleton & Lange.
- Klein R, Elvin BEK, Moss SJ, Cruickshanks KJ. Ten year incidence of gross proteinuria in people with diabetes. *Diabetes* 1995; (44): 916-923
- Sawicki PT, Didjurgeit U, Mulhauser I, Bender R, Heinemann L & Berger M. Smoking is associated with progression of diabetic nephropathy. *Diabetes Care* 1994; 2 (17) : 126-131.
- DCCT Research Group. The Effect of intensive treatment of diabetes on the development and progression of long term complications in IDDM. *The New England Journal of Medicine* 1993; 329: 977-986
- Gall MA, Hougard P, Jojnsen KB, Parving HH. Risk factors for development of incipient and overt diabetic nephropathy in patients with NIDDM prospective, observational study. *British Medical J*; 1997; 314 : 783-788.
- Schmitz A, Vaeth M, Mogensen CE. Systolic blood pressure relates to the rate of progression of albuminuria in NIDDM. *Diabetologia* 1994; 37 : 1251-1258.
- Neil A, Hawkins M, Polok M, Thorogard M, Cohen D, Mann J. A prospective population-based study of microalbuminuria as a predictive of mortality in NIDDM. *Diabetes care*.1993; (16) 7 : 996-1003.
- Microalbuminuria Collaborative Study Group, U.K. Risk factor for development of microalbuminuria in IDDM patients : A cohort study. *British Medical J*. 1993; 306 :1235-1240.
- Powrie JK, Watts GF, Ingham JN, Taub NA, Talmud PJ, Shaw KM. Role of glycaemic control in development of microalbuminuria in patients with insulin dependent diabetes. *British Medical J* 1994; 309: 1608-1612.