Journal of the Formosan Medical Association (2017) xx, 1–9

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfma-online.com

Original Article

Factors associated with diabetic nephropathy in children, adolescents, and adults with type 1 diabetes

Chi-Yu Huang [a,b,c], Wei-Hsin Ting [a,b,c], Fu-Sung Lo [d,e], Jeng-Daw Tsai [c,f,g,h], Fang-Ju Sun [b,i], Chon-In Chan [a], Ya-Ting Chiang [a], Chao-Hsu Lin [j], Bi-Wen Cheng [j], Yi-Lei Wu [k], Chen-Mei Hung [l], Yann-Jinn Lee [a,c,h,i,m,*]

[a] *Department of Pediatric Endocrinology, MacKay Children's Hospital, Taiwan, ROC*
[b] *MacKay Junior College of Medicine, Nursing, and Management, Taiwan, ROC*
[c] *Department of Medicine, Mackay Medical College, Taiwan, ROC*
[d] *Department of Pediatrics, Chang Gung Memorial Hospital, Taiwan, ROC*
[e] *College of Medicine, Chang Gung University, Taiwan, ROC*
[f] *Department of Pediatric Nephrology, MacKay Children's Hospital, Taiwan, ROC*
[g] *Department of Pediatrics, Taipei Medical University Hospital, Taipei, Taiwan, ROC*
[h] *Department of Pediatrics, School of Medicine, College of Medicine, Taipei Medical University, Taiwan, ROC*
[i] *Department of Medical Research, MacKay Memorial Hospital, Tamsui District, Taiwan, ROC*
[j] *Department of Pediatrics, Mackay Memorial Hospital, HsinChu Branch, Taiwan, ROC*
[k] *Department of Pediatric Endocrinology and Metabolism, Chuanghua Christian Children's Hospital, Taiwan, ROC*
[l] *Department of Pediatrics, Hsinchu Cathay General Hospital, Taiwan, ROC*
[m] *Institute of Biomedical Sciences, Mackay Medical College, Taiwan, ROC*

Received 16 March 2017; received in revised form 12 September 2017; accepted 28 September 2017

KEYWORDS
Type 1 diabetes;
Diabetic nephropathy;
Microalbuminuria;
Macroalbuminuria;

Abstract *Backbroud/Purpose:* Microalbuminuria and macroalbuminuria are markers of diabetic nephropathy (DN). The purpose of this study was to unravel the risk factors for DN in the young patients with type 1 diabetes (T1D).
Methods: 341 patients (160 males) with T1D diagnosed at the age 7.6 ± 4.0 years with disease duration 11.5 ± 6.5 years were assessed. Among them, 185 were young adults (aged 18.0–36.2 years). Urinary albumin creatinine ratio (UACR) was checked on morning spot urine.

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

* Corresponding author. Department of Pediatric Endocrinology, MacKay Children's Hospital, Laboratory of Molecular Medicine, Department of Medical Research, MacKay Memorial Hospital, 45 Minsheng Rd., Tamsui District, New Taipei City 25160, Taiwan, ROC. Fax: +886 2 28098746.
E-mail address: yannlee@mmh.org.tw (Y.-J. Lee).

https://doi.org/10.1016/j.jfma.2017.09.015

HbA1c

Microalbuminuria and macroalbuminuria were defined as a UACR of 30−300 mg/g and >300 mg/g, respectively, in at least 2 consecutive specimens.
Results: 50 (14.7%) patients were classified as microalbuminuria and 13 (3.8%) as macroalbuminuria. In all patients, multivariate logistic regression revealed that the most significant risk factors were average HbA1c (%), OR (95% CI) = 1.76 (1.37−2.25), $P = 0.002$); and male sex, OR = (odd ratio 2.31 (1.19−4.46), $P = 0.013$). In adult patients, the most significant factors were average HbA1c, OR = 1.74 (1.32−2.31), $P = 0.003$; and systolic blood pressure, OR = 1.06 (1.01−1.11), P = 0.011. Survival analysis showed average HbA1c levels significantly influenced the development of DN.
Conclusion: The most important risk factors for DN were average HbA1c and age. When microalbuminuria is detected, proper treatment with ACEIs or ARBs and improving glycemic control can delay progression of DN.

Introduction

Diabetic nephropathy (DN) occurs in 20−40% of patients with diabetes and is a major cause of end-stage renal disease (ESRD).[1] The impact on life quality is serious and the cost of treatment is high for patients with ESRD. Chronic renal disease also associated with premature mortality in patients with diabetes. Since most patients with type 1 diabetes (T1D) were diagnosed in childhood or adolescents, early detection and prevention of DN are necessary.

Microalbuminuria and macroalbuminuria have been established as important markers of early and progressive kidney disease in diabetes. Annual exam of urine albumin to creatinine ratio is suggested for patients with diabetes. Early detection of microalbuminuria and proper treatment may reverse or delay the progress of diabetic kidney disease.[2]

The incidence of T1D varies in different ethnics, it is much lower in Asians than in Caucasians. The studies on DN in T1D are also rare in Asia. T1D is present in less than 1% of the diabetic population in Taiwan.[3] However, the incidence of newly-diagnosed T1D patients is increasing,[3−5] and about 90% are due to autoimmune destruction of β-cells.[6] The cumulative incidence of ESRD in T1D patients is significantly higher in patients > 30 years old than in patients < 30 years old in Taiwan (10.25% vs. 3.57%).[7] Unraveling the pathogenesis of microalbuminuria and macroalbuminuria in the young helps us formulate strategies to effectively treat and even prevent DN and stop ESRD.

We investigated a cohort of patients with T1D diagnosed before age 18. Most of them were younger than 30 years. The aims of this study were to analyze the prevalence of DN and to identify risk factors for early nephropathy.

Research design and methods

A cohort of 341 patients with T1D diagnosed before age 18 was prospectively followed at the clinic every 3 months. They were 160 males and 181 females. Their mean age ± SD at diagnosis was 7.6 ± 4.0 (ranged 1.1−17.9) years, age at the last assessment 19.1 ± 7.0 (4.4−36.2) years, and follow-up period (disease duration) 11.5 ± 6.5 (1.0−34.5) years. Among them, 185 had been young adults (aged 18.0−36.2 years) at the last assessment. The age at the last assessment is the age at diagnosis plus disease duration till the last assessment. The patients were grouped according to their age at the last assessment: children < 10 years, adolescents ≥10 years and <18 years, adults ≥ 18 years.[8]

Urinary albumin creatinine ratio (UACR) was annually checked on morning spot urine. DN was defined as persistent UACR ≥ 30 mg/g.[9] The patients were classified into 3 groups as normal albuminuria, microalbuminuria, and macroalbuminuria by UACR according to NKF-KDOQI (National Kidney Foundation−Kidney Disease Outcomes Quality Initiative).[10] (1) Normal albuminuria was defined as UACRs were persistently <30 mg/g. An episode of UACR > 30 mg/g which spontaneously recovered within one year was also categorized into this group; (2) Microalbuminuria was defined as a UACR of 30−300 mg/g in at least 2 consecutive specimens in a 3-month interval; (3) Macroalbuminuria was defined as a UACR of >300 mg/g persistently in at least 2 consecutive specimens in a 3-month interval.[9] As soon as microalbuminuria was detected and confirmed, ACEI/ARB was administered with follow-ups of UACR.

A blood sample was drawn for biochemistry annually after 8−10 h of overnight fasting.[11] Biochemistry includes serum triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol, and creatinine. Estimated glomerular filtration rate (eGFR) was calculated by Schwartz formula for children and adolescent,[12,13] or MDRD (the modification of diet in renal disease) study equation for adult (age ≥ 18 years).[14,15] Blood pressure, weight, and height were measured at each clinical visit. Systolic blood pressure and diastolic blood pressure were measured after patients remained seated for at least 5 min.[16] The data of blood pressure, weight, height and biochemistry were from the last assessment unless otherwise noted. Their medications were also recorded. The glycemic control was monitored using daily self-monitoring of blood glucose and blood HbA1c every 3−4 months from diagnosis. A year was defined as 365.25 days. An annual mean HbA1c level was the mean of all HbA1c levels in a year period excluding those within 3 months after diagnosis. An average HbA1c value was the average of all annual mean HbA1c levels. The patients were

Please cite this article in press as: Huang C-Y, et al., Factors associated with diabetic nephropathy in children, adolescents, and adults with type 1 diabetes, Journal of the Formosan Medical Association (2017), https://doi.org/10.1016/j.jfma.2017.09.015